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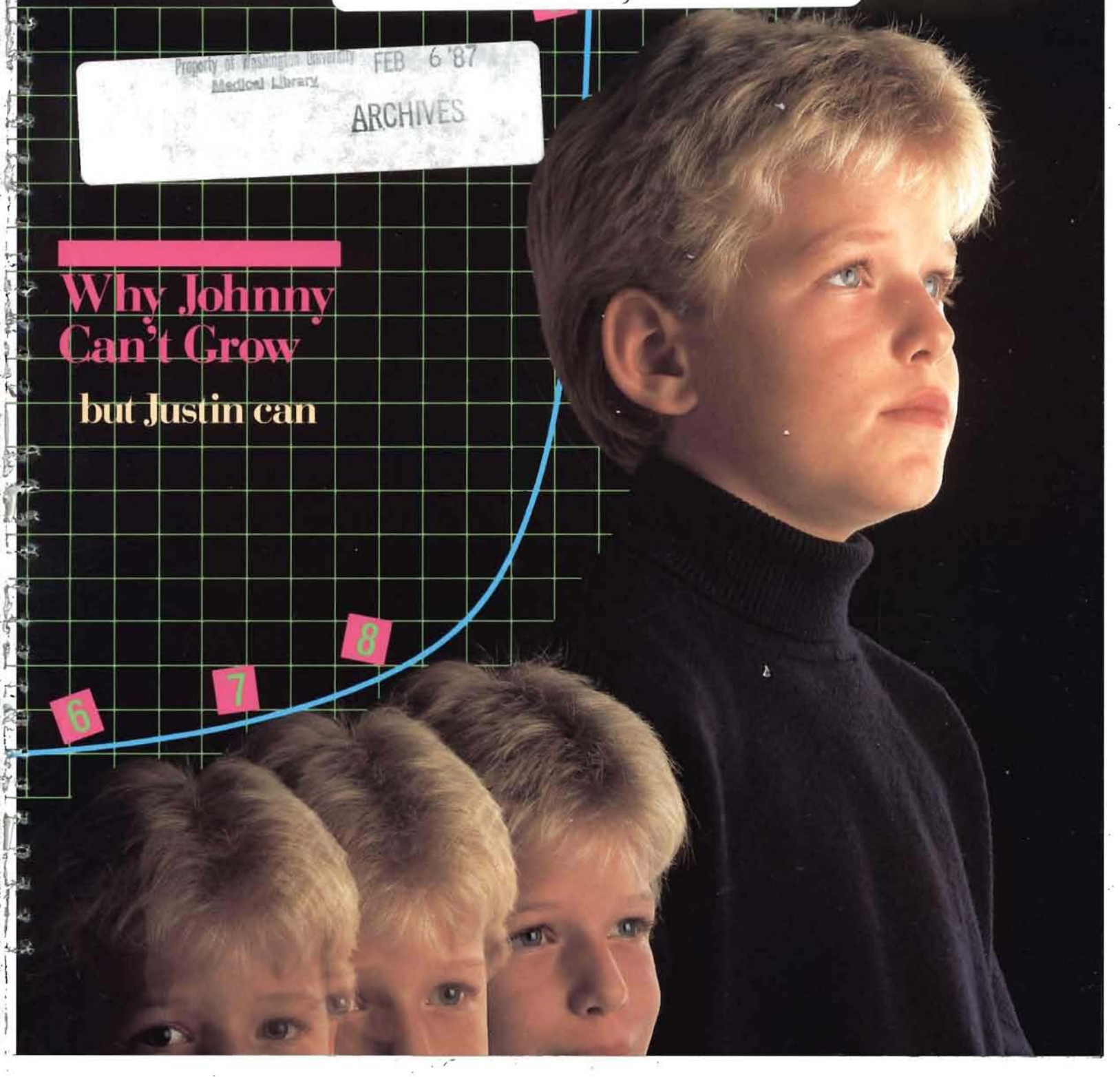
WASHINGTON UNIVERSITY SCHOOL OF MEDICINE WINTER 1986

OUTLOOK

Why Johnny Can't Grow but Justin can



Children who attend day-care centers run an increased risk of exposure to the highly contagious bacterium Haemophilus influenzae type b (Hib), a common cause of meningitis — a severe infection of brain and spinal cord membranes. A fortunate meningitis recoverer, Matthew Martin (right), plays at a St. Louis area day-care center with Andrew Burns, a recent participant in clinical trials for a new vaccine against Hib directed by Dan M. Granoff, M.D., at Washington University School of Medicine. *See story, page 4.*

OUTLOOK

Volume XXIII, Number 4 Winter 1986

On The Cover:

Human growth hormone therapy at the School of Medicine helps otherwise growth-deficient children obtain normal size.

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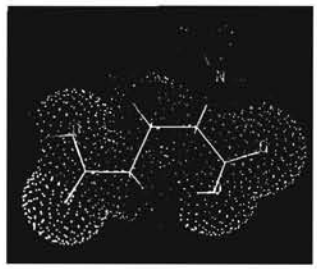
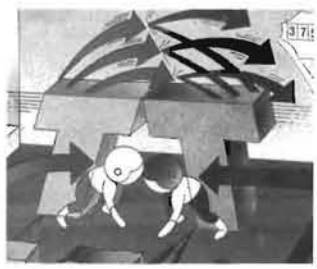


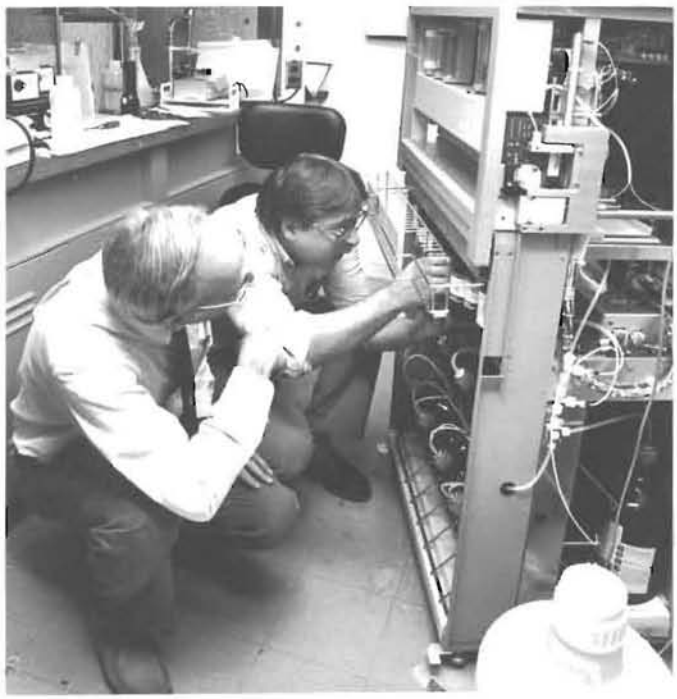


Nemeth Muscles Up Research

Patti M. Nemeth, Ph.D., associate research professor of neurology and of anatomy and neurobiology, has been awarded more than $526,000 in two grants from the National Institutes of Health.

The first award is from the National Institute of Neurology and Communicative Disorders and Stroke and will fund a project on the biochemistry and physiology of single axons and the set of muscle fibers they simulate. Nemeth and her team have developed a technique for measuring energy metabolism, anatomical arrangement and physiological properties of these individual "motor units." The technique enables Nemeth to compare precisely the biochemical and physical make-up of muscle and the physiological characteristics of its nerve.

The second award is from the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases for a study of neural influences on the biochemistry of single muscle fibers. In this research, Nemeth tests the extent to which neural and non-neural factors — such as hormonal factors — affect muscle during development, and how fully mature muscles can be altered by long-term exercise or by programmed contractions induced with artificial stimulation. ■



Gregory A. Grant, Ph.D., assistant professor of biochemistry and medicine, explains the finer points of the protein chemistry lab's new peptide synthesizer to Carl Frieden, Ph.D.

New Peptide Synthesizer

A $140,000 gift from the Whitaker Charitable Foundation has enabled the Department of Biological Chemistry to purchase a new peptide synthesizer for its protein sequencing facility.

Serving as a companion instrument to the vapor phase protein sequencing system, which was purchased last year from an earlier Whitaker foundation gift, the peptide synthesizer is expected to open up many research possibilities at Washington University, according to Carl Frieden, Ph.D., professor and interim head of the department.

The instrument will be especially useful in Frieden's work, which was recently awarded distinguished MERIT status by the National Institute of Diabetes and Digestive Kidney Diseases. Such designation provides a few outstanding investigators with long-term stable support, allowing them to continue their investigations without many of the administrative burdens associated with the preparation and submission of grant applications.

"With this new instrument, we can synthesize peptides against which antibodies could be prepared and targeted to specific malignant cells and not to other cells," Frieden says. The new instrument should also aid investigation into cellular functions such as motility, cytoskeletal structure, endocytosis and cell division. Under the direction of Urban C. Bergbauer, trustee, the foundation has donated more than $500,000 to the department's protein synthesizing facility. ■

Hot Stuff on Cells

Joseph L. Roti Roti, Ph.D., associate professor of radiology, has been awarded $200,657 from the National Cancer Institute in the form of two research grants to study the effects of hyperthermia — the use of heat to shrink cancerous tumors — on cell structure.

The first grant will allow Roti Roti and co-researchers to study the effects of radiation and hyperthermia on nuclear organization and function. In particular, the six-year study is aimed at determining whether or not heat and x ray-induced changes inhibit cell reproduction.

The second grant will enable him to study the correlation between heat-induced changes in nuclear proteins and growth delay in cancerous tumors. "Our overall goal," he says, "is to explain the biological mechanism of therapeutic methods."

Roti Roti was an associate professor of radiology at the University of Utah School of Medicine in Salt Lake City before being appointed to his present position at the university in 1985. He is the recipient of a number of research grants in cell kinetics and structure and has contributed nearly 50 publications to the literature of biophysics. ■

New Hib Vaccine

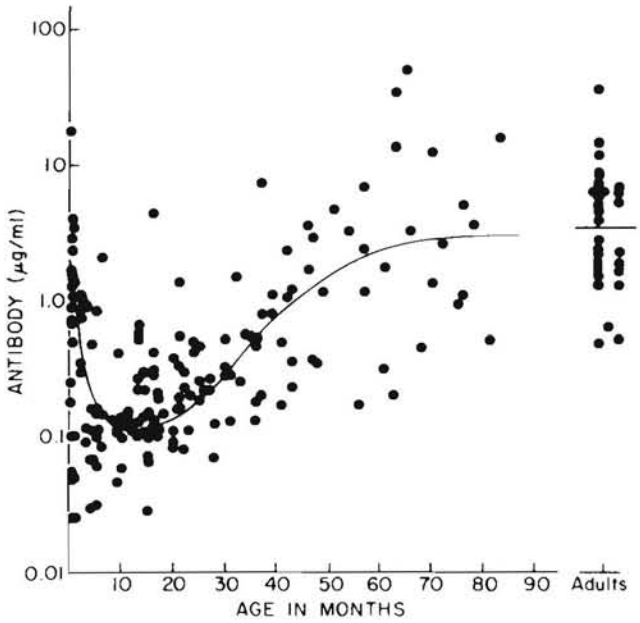
Clinical trials of a new vaccine against Haemophilus influenzae type b (Hib) — a bacterium responsible for bacterial meningitis and a number of other life-threatening childhood illnesses — show that the new vaccine for the first time affords protection in infants from two to six months of age.

"This study marks the first time any vaccine has produced antibody levels considered capable of protecting infants as young as two months," says Dan M. Granoff, M.D., professor of pediatrics and associate professor of microbiology and immunology.

"Of the 63 children we immunized, 25 were 8–17 months old and 38 were younger than six months," Granoff says. "In most cases, even a single injection raised antibody levels among infants younger than six months higher than those produced by any other Hib vaccine."

Robert Daum, M.D., head of pediatric infectious diseases at Tulane University, calls Granoff's work "groundbreaking. The exciting thing is that this new vaccine looks fantastically immunogenic, capable of protecting young children at their peak susceptibility to the disease." Daum is a member of the American Academy of Pediatrics committee on infectious diseases.

"Most of the infants in our study showed further increases in antibody after a second injection," Granoff continues. "We're encouraged by these results because a vaccine that is effective in this key age group can confer Hib immunity to millions of children who aren't protected by the currently licensed vaccine, or who'd be poorly protected even after two doses of the other unlicensed, investigational Hib vaccines tested to date."



Dan M. Granoff, M.D.'s, research team determined the levels of antibody against Hib bacteria in normal subjects. Their new vaccine is effective in children most vulnerable to Hib disease, those younger than 24 months.

The vaccine currently used against Hib disease, which was licensed in 1985 and is produced by several companies, contains a purified piece of the Hib bacteria's outer coating, which is composed of linked sugars called polysaccharides. Thus the currently licensed vaccine is known as Hib polysaccharide vaccine or Hib PS.

In a large National Institutes of Health-sponsored clinical trial, this Hib PS vaccine produced significant antibody levels in older children but was found to be totally ineffective in infants less than 18 months old, the age group at highest risk for Hib disease.

In 1984, representatives from Merck Sharp and Dohme asked Granoff's team of seasoned investigators — who'd tested the Hib PS vaccine and who were experienced in evaluating responses to immunization — to test a new vaccine: an Hib PS protein conjugate.

In the new vaccine, Hib PS is linked to a protein purified from a meningococcus bacteria which, like Hib, is also known to cause meningitis. This conjugation of PS to protein greatly enhances antibody response within infants. In addition to choosing the correct protein to act as a spark plug for Hib PS, researchers also found a unique way to link Hib PS and protein without disturbing the Hib PS bacteria-fighting activity.

In spite of promising results, which were recently published in the prestigious British medical journal *Lancet*, work must still be done before the new vaccine can be licensed. "We have to determine the optimal dose and immunization schedule," says Geoffrey A. Weinberg, M.D., a research fellow and co-author of the *Lancet* article. "We're not yet sure of the precise level of antibody required to provide protection, and we have to be sure that the antibody produced by this vaccination will last."

Granoff's team has already immunized more than 100 additional infants since completion of the *Lancet* study. In this second trial, infants again produced good antibody levels with few side effects.

Once the exact dose and schedule are refined, the next step is a series of trials in which thousands of children are vaccinated and monitored for several years to make sure they remain immune to Hib. These trials will also detect any safety problems that might not have appeared in previous studies.

"We can't yet swear by the Hib PS-protein conjugate vaccine," Weinberg says, "but it looks good, very good." ■

New Alumni President

Donald G. Sessions, M.D. '62, has been named president of the Washington University Medical Center Alumni Association. An expert on the surgical treatment of head and neck cancers, Sessions is professor of otolaryngology and director of resident training for the otolaryngology department.

Sessions graduated from the School of Medicine in 1962. After completing an internship and residency in surgery at Vanderbilt Hospital in Nashville, Tennessee, he returned to Washington University for a residency in otolaryngology. Following military service at the U.S. Air Force Hospital in Anchorage, Alaska, he was named assistant professor of otolaryngology at Washington University in 1970.

Sessions is on staff at Barnes, Children's and Jewish hospitals. He is a member of a number of professional organizations, including fellowship in the American College of Surgeons, the American Academy of Otolaryngology — Head and Neck Surgery, the American Academy of Facial Plastic and Reconstructive Surgery and the American Society for Head and Neck Surgery. He has published numerous journal articles in his field and is the author of a textbook, *Atlas of Laryngeal Surgery*. Sessions has a special interest in well-being and the doctor-patient relationship and is currently doing research in this area. ■

Donald G. Sessions, M.D. '62

Perry Honored for Teaching Good Heart Habits

H Mitchell Perry Jr., M.D., professor of medicine and director of the hypertension division, has received the Louis B. Russell Jr. Memorial Award from the American Heart Association.

The award recognizes Perry for outstanding achievement in educating minorities about lifestyles that are healthy for the heart. Louis Russell, a black Indianapolis teacher, received a transplanted heart in 1968 and was an energetic volunteer for the American Heart Association until his death in 1974.

Perry was cited for a project he created to help solve a major problem in the St. Louis area: identifying young, black males with uncontrolled hypertension who face potentially fatal medical problems. The program Perry developed began in 1982 and called for door-to-door canvassing of minority communities to locate and treat people with high blood pressure. He directed the project, which was funded by the St. Louis chapter of the American Heart Association and was a cooperative community effort involving a number of educational institutions and health organizations.

Perry has been director of the hypertension division at the School of Medicine since 1957. He also serves as director of the hypertension program at the St. Louis Veterans Administration Hospital, and as physician coordinator for the VA's national hypertension program.

He is currently directing the St. Louis section of a 16-center national study called the Systolic Hypertension in the Elderly Program (SHEP). The study is designed to learn whether lowering systolic blood pressure with drugs will decrease heart attacks and strokes. It also investigates whether medication can favorably affect memory and mental powers in people aged 60 and older.

St. Louis researchers plan to enroll at least 300 men and women aged 60 and older with isolated systolic hypertension by March 1987. More than 200 volunteers are participating in the local study. More information about SHEP is available through the SHEP office, 314-367-2547. ■

Logan Gives New Twist to Wrists

Samuel E. Logan, M.D., Ph.D., assistant professor of plastic and reconstructive surgery, has received a three-year grant of $150,000 from the Whitaker Foundation to continue investigating the complex anatomy of the wrist. In the future, he hopes to evaluate and design improved wrist operations and possibly an improved wrist prosthesis.

Logan's research is a collaboration among a number of investigators in the Division of Plastic Surgery and Michael Vannier, M.D., associate professor of radiology.

Logan is assistant professor of mechanical engineering at Washington University School of Engineering and Applied Science. ■

New Director of Alumni and Development Programs

The School of Medicine bids farewell to Jack Siefkas, director of medical development programs, and welcomes his replacement, Mark W. Bates.

Siefkas, who served as director of medical alumni and development programs for four years, will be doing development work at the University of Kansas for a Chicago-based consulting firm.

Bates comes to the School of Medicine from the Office of University Relations at the Hilltop Campus, where he served as assistant vice chancellor and director of special development programs. Bates came to the university in 1985 with nearly 27 years of institutional advancement experience in Chicago, having served as vice president and executive secretary to the board of trustees at Illinois Institute of Technology, and executive vice president of the American Fund for Dental Health.

A journalism graduate from Northwestern University, Bates has also served as vice president for institutional advancement at the College of St. Francis in Joliet, and vice president for a development consulting firm whose clients included the Chicago Symphony Orchestra. ■

Nicholas T. Kouchoukos, M.D, uses an autotransfusion system he designed to re-introduce a patient's own blood after open-heart surgery.

Blood Recycling

Recycling a patient's own blood during and after open-heart surgery can, in some cases, completely eliminate the need for donor blood.

In a recent study of this method conducted by Nicholas T. Kouchoukos, M.D., John M. Schoenberg Professor of Cardiovascular Surgery, and William G. Marshall Jr., M.D., assistant professor of surgery, 32 percent of 115 coronary artery bypass graft patients needed no donor blood. Among those under the age of 70, 38 percent received no donor blood.

"This auto-transfusion system has proven to be safe, economical and simple to use and results in the savings of substantial amounts of red blood cells and platelets," Kouchoukos says.

The auto-transfusion system involves a fairly simple apparatus that collects and filters blood lost as chest drainage early after surgery. That blood is gradually reintroduced to the patient's body through an infusion pump during the first 18 hours after surgery, salvaging an average of three units of red blood cells. To date, auto-transfusion has not been found to be associated with any significant complications, such as infection or bleeding requiring re-operation.

"Because of concerns from both potential blood donors and potential recipients concerning AIDs, as well as hepatitis and other disorders that can be transmitted by blood transfusions, an auto-transfusion system that can minimize the use of donor blood has additional relevance," Kouchoukos adds.

"While the risk of contracting one of these disorders is extremely low, these anxieties have placed pressure on the blood supply and an understandable reticence among some patients to accept donor blood. We cannot guarantee that no donor blood will be used, but we know that eliminating or minimizing its use has positive effects both on the blood supply and on patient morale, and does reduce the risk of contracting any of these diseases." ■

Drug Use Before 15

Youth who begin using drugs before age 15 are more likely to develop severe drug abuse or dependence than those who postpone drug use until a later age, according to a study by internationally recognized drug abuse expert Lee N. Robins, Ph.D., professor of sociology in psychiatry.

According to her study, of all the participants who used drugs five times or more, 25 percent of men and 16 percent of women developed a drug disorder (abuse or dependence). When use began before the age of 15, however, the figures more than doubled: 51 percent of the men and 39 percent of the women developed drug disorders. As first drug use was delayed, the risk of developing a drug disorder decreased, the study showed.

"We don't know yet why early use of drugs is so dangerous, but one reason may be that it makes kids drop out of school," Robins suggests. "With no skills, they have no way of re-entering society when they give up drugs, as many will by their early 20s. The problem is how to prevent others from starting drugs without irreparably damaging the kids already involved with drugs."

Not only is under 15 the most dangerous age for onset of drug use, it also is the easiest time to intervene, Robins says. "One of the advantages of working with younger kids is that it is easier to monitor their behavior. Prohibiting kids from

leaving school at lunch is more acceptable to a 12- to 13-year-old than to a 17-year-old. The restrictions are more readily accepted by younger kids. Because the law says children have to stay in school until they are 16, it is much safer to confront younger kids; older kids may just drop out rather than accept the strict new rules."

Her study, "Age of Onset of Drug Use as a Factor in Drug and Other Disorders," co-authored with Thomas R. Przybeck, Ph.D., a statistical data analyst, was prepared for the National Institute of Drug Abuse. It was published by the Department of Health and Human Services in "Etiology of Drug Abuse: Implications for Prevention."

Robins' study involved personal interviews with participants aged 18 to 35 in New Haven, Conn.; Baltimore; and St. Louis. Respondents were interviewed first between 1979 and 1981 and reinterviewed a year later.

The study shows that sex, race and education are only weakly related to drug disorders, with slightly higher rates for males, whites and inner-city residents. Beginning drug use before age 15 predicted an increased risk of drug disorders, particularly of a severe type. Early onset of use was also associated with more alcoholism and antisocial personality in later life.

The researchers looked for factors that could predict drug use. "Early behavior problems are very good predictors of substance abuse," Robins says, "although many drug abusers are apparently normal children."

The leading predictors of onset of drug use are: early drunkenness, school discipline problems, depression, stealing, vandalism and truancy, the study shows. Broken homes also predicted drug abuse, but were much less important that the child's own behavior.

Robins has a new grant from the National Institute of Drug Abuse and the National Institute of Mental Health to study whether drug abuse by normal youth differs in character and consequences from abuse by those with a troubled behavior history. "Because only 50 percent of the drug users had earlier behavior problems, we want to know what the pathways are to drugs for kids who do not have behavior problems," Robins says. ■

Cancer Society Elects Loeb

Virgil Loeb Jr. M.D. '44, professor of clinical medicine, has been elected President of the American Cancer Society.

Loeb succeeds Charles A. LeMaistre, M.D., of Houston, who served as the Society's President for the 1985-86 term.

During his tenure as president, Loeb plans to stress a message of hope concerning cancer. "Half of all cancer patients today are being cured," he says. "We have made remarkable progress during recent decades in detecting and treating cancer and in the understanding of the biology of cancer as well. Evidence seems to indicate that we have even greater prospects to prevent cancer by making careful choices in our lifestyles. For example, by choosing wisely what we eat and choosing not to smoke, we reduce our risk of cancer considerably.

"We in the American Cancer Society call such choices 'Taking Control,' and we have designed a program by that name to guide people in making value wise decisions relating to cancer risk. Urging Americans to take control of their lives by making educated choices in cancer detection, treatment and prevention will be our message during the year to come."

After receiving his M.D., Loeb completed internships, a fellowship and residency at hospitals in Missouri and Connecticut and a traineeship with the National Cancer Institute, returning to the university in 1950 as a Damon Runyon Research Fellow in Hematology.

Currently a member of the Board of Scientific Counselors of the Division of Cancer Prevention and Control of the National Cancer Institute and of the Institute of Medicine of the National Academy of Sciences, Loeb has also served on numerous committees of the American Cancer Society and other organizations. He joined the National Board of Directors of the Society in 1979, and is a former president of both the ACS Missouri Division Board and the St. Louis Unit Board.

His professional memberships include the American Board of Internal Medicine, the American College of Physicians, the American Association for Cancer Research and the American Society of Clinical Oncology.

A native of St. Louis, Dr. Loeb is married to the former Lenore Harlow. They have two daughters and two sons. ■

Virgil Loeb Jr., M.D., talks with his patient and cousin, Fay Barker, in Mallinckrodt Institute of Radiology's Cancer Information Center.

Glutamate As TRANSMITTER AND TOXIN

BY PAUL DUSSEAULT

It happens in Alzheimer's disease, Huntington's chorea, epilepsy and other well known neurobiological disorders. It happens in cerebral palsy, cardiac arrest, stroke, hypoglycemia and other cases where the brain's supply of precious oxygen or glucose is interrupted. It happens in head injuries from football games, stairway tumbles and auto accidents.

Nerve cells in the brain die and are not replenished — the brain is damaged.

But two decades of research by John W. Olney, professor of psychiatry and neuropathology, have brought us closer to understanding the mysterious causes for such brain damage, and accumulating evidence suggests that novel drugs may soon be in the kits of physicians, even paramedics, to prevent nerve cells from dying in at least some of these conditions.

This is not a story of a medical breakthrough. There were no flashes of light, no cries of "Eureka!" It was more of a medical "wearthrough," a tedious trek towards a new understanding of neuropathological processes that began in 1968.

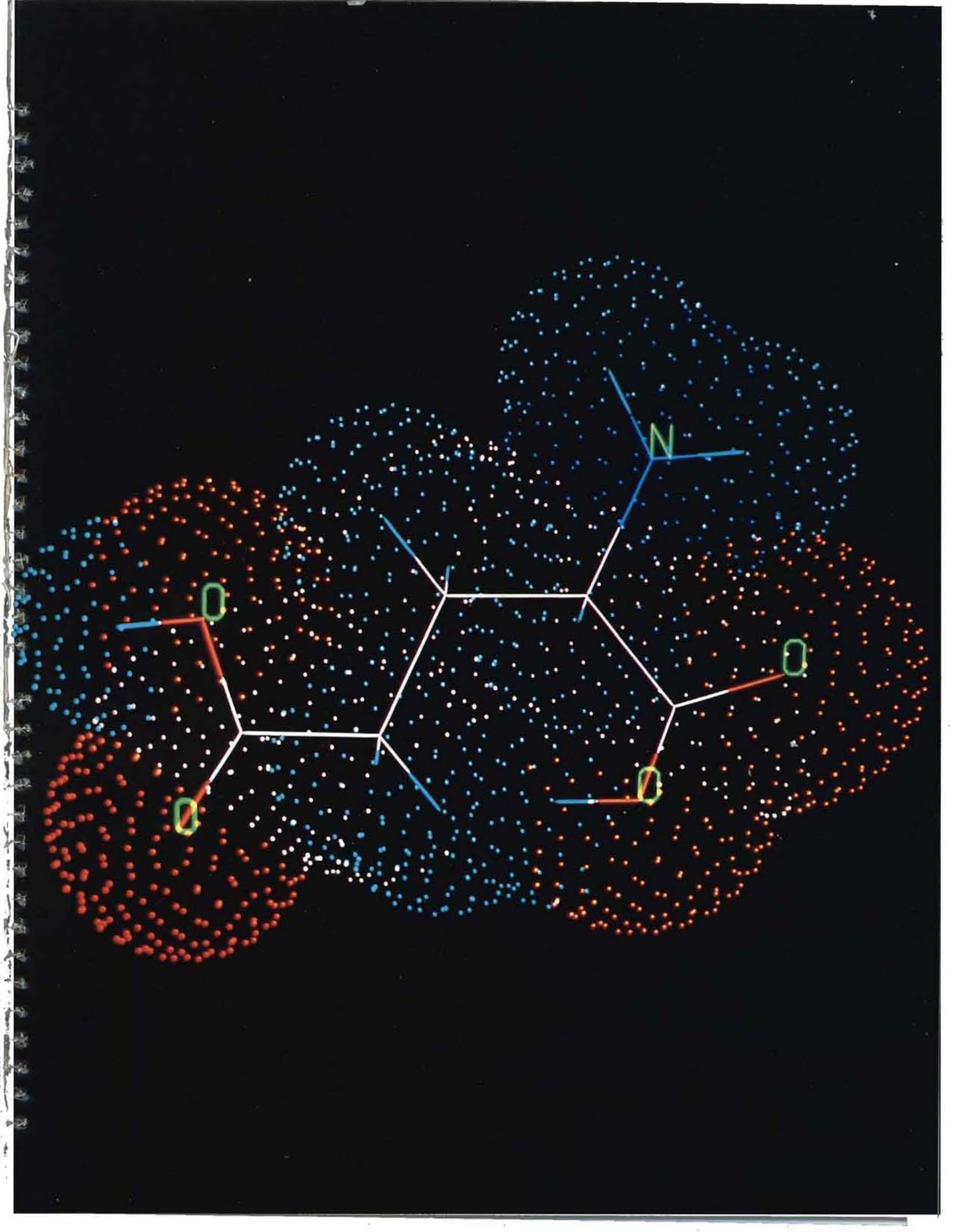
Prior to that time, a common amino acid called glutamate (Glu), which is found in high concentration in brain, had been shown to have an excitatory effect on central neurons. Paradoxically, this same substance also was found to cause the degeneration of nerve cells in the immature retina of baby mice, when injected under the skin.

As a resident at Washington University School of Medicine in the late 1960s, Olney confirmed Glu's damaging effects on immature mouse retina using both light and electron microscopy. Then he found that treatment of mice with Glu in infancy caused them to have a grossly abnormal body constitution as they grew to adulthood — they became obese, short and often sterile. By 1969 he had traced the cause of these developmental abnormalities to a toxic action of Glu on nerve cells in the hypothalamus, a brain region that exerts regulatory control over growth and development. At this point he knew that he was in hot pursuit of something very intriguing: If Glu occurs naturally in high concentrations throughout the central nervous system, how can it also be a toxin that can kill nerve cells?

In the ensuing decade, Glu became recognized as an exceedingly important substance in the brain. Not only is it a major building block in the formation of important brain peptides and proteins, but it also is a neurotransmitter that excites central neurons, thereby mediating information transfer from one cell to another. Indeed, it is currently believed to be the neurotransmitter released at the majority of excitatory synapses in the central nervous system. Recognition of Glu as mediator of vitally important functions in brain made the enigma confronting Olney all the more challenging. The paradox: A substance integral to the brain's information processing functions has the potential of killing brain cells.

Major progress in unraveling the mystery was achieved by studying a large number of Glu analogs. Prominent Australian electrophysiologists, David Curtis and J.C. Watkins, found that some Glu analogs reproduce the neuroexcitatory effects of Glu, and some do not. In 1970, Olney demonstrated that the same Glu analogs that reproduce the excitatory effects of Glu also reproduce its neurotoxic effects. This basic observation has been confirmed repeatedly. Thus, the excitatory mechanism by which Glu passes messages from one cell to another is believed to be the same mechanism by which it kills nerve cells. "Glu might be viewed as a Jekyll and Hyde molecule," Olney says. "When present inside the nerve cell in normal concentrations, it is a benign substance that plays exceedingly important roles in brain physiology; if released from the nerve cell and not immediately taken back up, it interacts persistently with excitatory receptors on the external surface of the nerve cell and, in essence, excites the cell to death." To describe this unique duality, Olney coined the term "excitotoxin," a term which is now in common use among neuroscientists.

The most immediate impact of this discovery was its research applications. Before Olney's contribution, researchers studying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brain function used a method that seems quite crude by today's standards. A wire was inserted into the brain of an anesthetized animal, and a given area of the brain was destroyed when electric current was passed through the wire. Any loss of function or change in behavior was tentatively attributed to the cells destroyed.

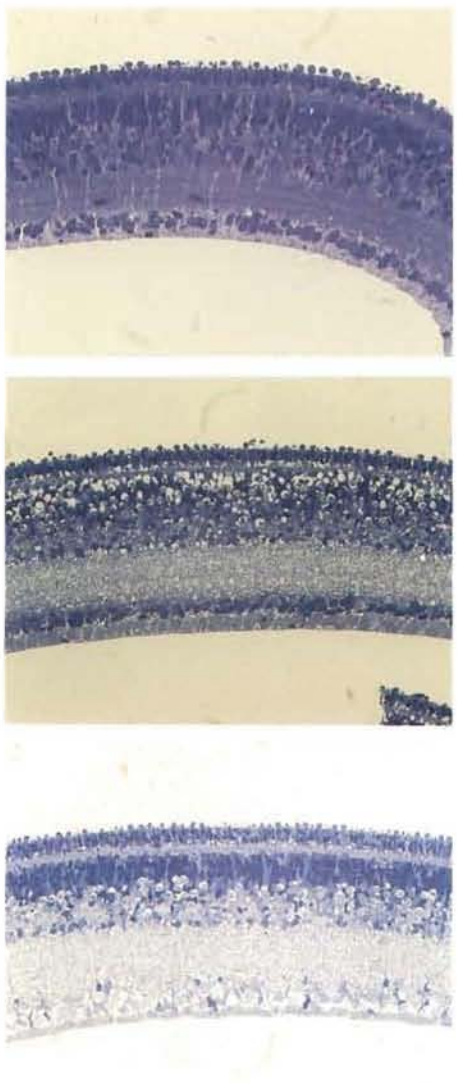
"The trouble with this method," Olney says, "is that it destroys everything in the area, including fibrous tracts that interconnect other brain regions. Sure, you can observe loss of function, but you cannot confidently attribute it to loss of the targeted cells; it might reflect the fact that fibers interconnecting other cells have been severed." Excitotoxins act at excitatory receptors on the surface of the target nerve cell, but fibers of passage are not damaged because they do not have such receptors. Olney's research has resulted in the identification of numerous excitotoxic analogs of Glu that are much more powerful than Glu and interact selectively with specific Glu receptor subtypes. "By carefully choosing the Glu analog that matches the receptors on the cell types targeted, researchers can destroy nerve cells with greater selectivity," says Madelon T. Price, Ph.D., research assistant professor of neurobiology in psychiatry, who joined Olney's research team in 1974.

The excitotoxin approach provides more reliable results than could be obtained with the old electric current method. "It's a sort of chemo-surgery," says Olney, "that allows one to draw more specific conclusions with regard to which nerve cells are responsible for which functions."

The most dramatic impact of excitotoxin research is its potential clinical applications. In the early 1970s, Olney expressed the view that, given Glu's ubiquity in brain and striking neurotoxic potential, it would be surprising if Glu irregularity wasn't implicated by neurodegenerative diseases. "In fact, over the past five years researchers from all over the world have been reporting new evidence potentially linking the excitotoxic action of Glu to brain damage associated with epilepsy, stroke, cerebral palsy, Huntington's chorea, Alzheimer's disease and several other less well known neurological conditions," Olney says. "On the basis of very recent evidence, it has even been proposed that a defect in the Glu transmitter system might play a role in schizophrenia."

"We suspected early on that clinical applications would be found," Price says. "But the number of potential clinical applications turning up is rather bewildering."

Between nerve impulses the Glu is stored safely inside cells. During the transmission of a nerve signal, it is released from the cell in tiny amounts for a fraction of a second, then immediately taken back up so the excitatory receptors will not be excessively stimulated. The mechanisms responsible for gathering up Glu after it has performed its message-carrying function and returning it to the cell's interior are normally very efficient. However, under abnormal circumstances — for example, when the brain's supply of blood, oxygen or sugar is deficient — these mechanisms fail, and Glu begins to accumulate outside the cell. Breakdown of the delicate mechanisms that hold Glu in check can lead to a rush of excitotoxin — a glutamate tsunami — which floods numerous receptors with brain poison.



Some Glu analogs cause more damage to nerve cells than others. A series of three micrographs shows from top to bottom: undamaged retina, partial damage to retina from one Glu analog and extensive retinal damage from yet another Glu analog.

The role of Glu in the neuropathology of head trauma is not well understood, but there is basis for suspecting that physical trauma, such as an auto accident or even neurosurgical procedures, can cause a release of Glu from its storage compartments inside the cell. Glu has several "metabolic" functions in addition to its transmitter function. A common amino acid, it is ubiquitous as a component of proteins. Every brain cell contains much larger amounts of Glu than are necessary for transmitter purposes. It is thought that brain trauma results in the release of Glu from metabolic as well as transmitter storage compartments and, because receptors do not distinguish between metabolic and transmitter Glu, they are over-stimulated by excesses of either.

"If we could find a way to block Glu receptors," Price says, "we might be able to protect those cells from being killed and prevent a lot of brain damage."

According to Olney, it is not unrealistic to believe that Glu receptor antagonists will one day be used successfully to prevent brain damage from stroke.

Steven Rothman, M.D., assistant professor of pediatrics and neurology at Washington University, has contributed valuable evidence on this point. When nerve cells grown in culture are deprived of oxygen, they rapidly die; but Dr. Rothman has shown that they can be protected from death by adding a Glu receptor antagonist to the culture medium. Swedish investigators have shown that when the blood

Using a Glu analog to selectively destroy nerve cell groups known to be damaged in Alzheimer's disease, Olney and his colleagues have created an animal model of the disease's effects on memory.

In the behavioral lab at Shriner's Hospital, David Wozniak, Ph.D., research associate in psychiatry, tests the memory capacities of rats using a radial arm maze.

When he places a rat in the center of the maze, it is free to run down any of eight alleys, each leading to a chocolate chip. Once the rat has selected an alley, Wozniak uses string pulleys to close the trap doors to the other seven alleys; the remaining trap door is closed after the rat has returned to the center. After five seconds, the trap doors are re-opened and the process begins anew.

As it has already eaten the chocolate chips in the traveled alleys, the rat must enter a new alley to obtain its "chocolate fix." Wozniak observes how much time it takes for normal and brain-altered rats to remember and make eight "correct" alley choices out of nine.

Preliminary results have shown that it takes rats with analog-induced Alzheimer-like lesions considerably longer to achieve this criterion than it does normal rats, indicating the powerful and debilitating effects the lesions have on memory. ■

supply is cut off to certain portions of an animal's brain, there is an outpouring of Glu from brain cells. In the absence of oxygen, the mechanism responsible for taking Glu back into the cell stops working. Thus, Glu remains in contact with receptors for a prolonged period, and cells are destroyed. It has been shown in this type of animal model that cell death can be prevented by injecting a Glu receptor antagonist directly into vulnerable brain regions.

A major problem, until very recently, has been the fact that none of the known Glu receptor antagonists passes readily across blood brain barriers. However, Olney's research team recently identified agents that effectively block Glu neurotoxicity and can pass from the blood into brain. "We have found that such agents prevent brain damage associated with prolonged seizures," says Olney, "and I am optimistic that they will prove effective in preventing other forms of brain damage."

A special problem in preventing brain damage associated with stroke is that you can't get the receptor blocker to the part of the brain undergoing damage because the blood vessel feeding that brain region is plugged with a clot. With the use of new drugs that can quickly dissolve such clots, Olney believes that one of the first clinical applications of excitotoxin research may be in the management of stroke. "I can easily envision treating stroke patients with a combination of a blood clot dissolver and a Glu blocker," he says, "a sort of brain-saving cocktail."

Olney's team is also interested in applying Glu blocking agents to prevent brain damage associated with respiratory failure in newborns. Emergency measures usually restore spontaneous breathing, but lack of oxygen during the period of respiratory failure, even if relatively brief, can give rise to cerebral palsy. The prime suspect: cell damage caused by an accumulation of Glu at excitatory receptors. "If a Glu blocker were used at the first sign of trouble," Price says, "it may be possible to prevent that brain damage."

One of the most potent Glu blockers Olney has identified is phencyclidine (PCP), a psychedelic drug otherwise known as angel dust. Olney's team has shown that this ordinarily devastating drug and related agents powerfully protect nerve cells against the toxic action of Glu and also prevent brain damage of the type caused by seizures. Present evidence suggests that these agents also protect nerve cells from dying when the blood supply to the brain has been cut off. Thus, angel dust or related drugs may assume a new image one day as protectors of human health.

And, as angel dust is not only a powerful blocker of Glu receptors but produces, in normal individuals, two common manifestations of schizophrenia — hallucinations and delusions — Olney and his colleagues are becoming fascinated with the possibility that dysfunction of the Glu transmitter system might play a role in schizophrenia.

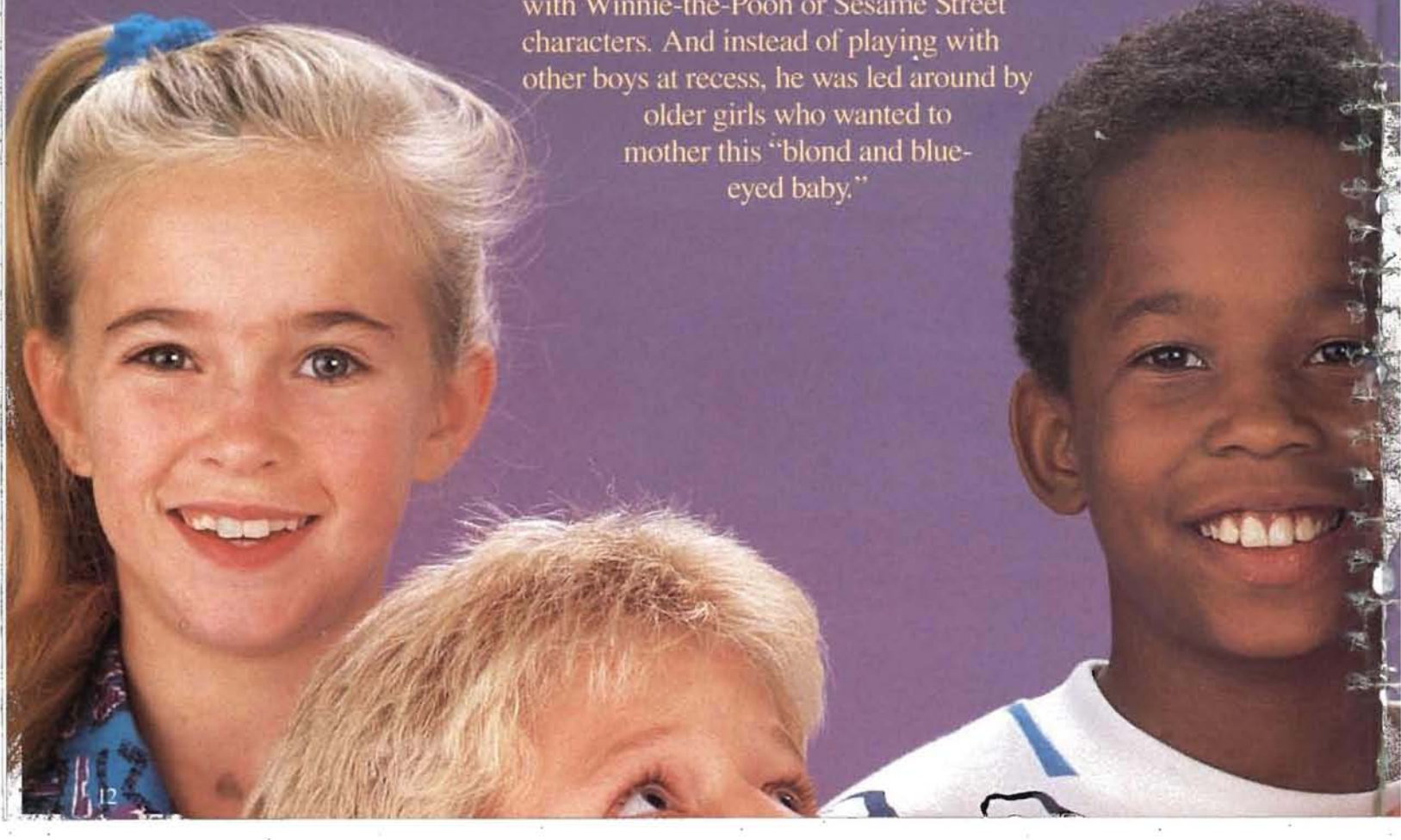
The list goes on. There is speculation implicating an excitotoxic mechanism in Huntington's chorea and Alzheimer's disease, both of which involve the death of specific nerve cells. Olney considers this relatively unlikely but he says, "Ten years ago, I could not have predicted that we would find an excitotoxin link to the brain damage associated with epilepsy, stroke, perinatal asphyxia or cardiac arrest." Researchers around the world are carefully studying the potential implications of recent findings in this new field of excitotoxicology — a field that can truly be considered Olney's brainchild, born and raised in his psychiatry laboratories at Washington University School of Medicine. ■

WHY JOHNNY

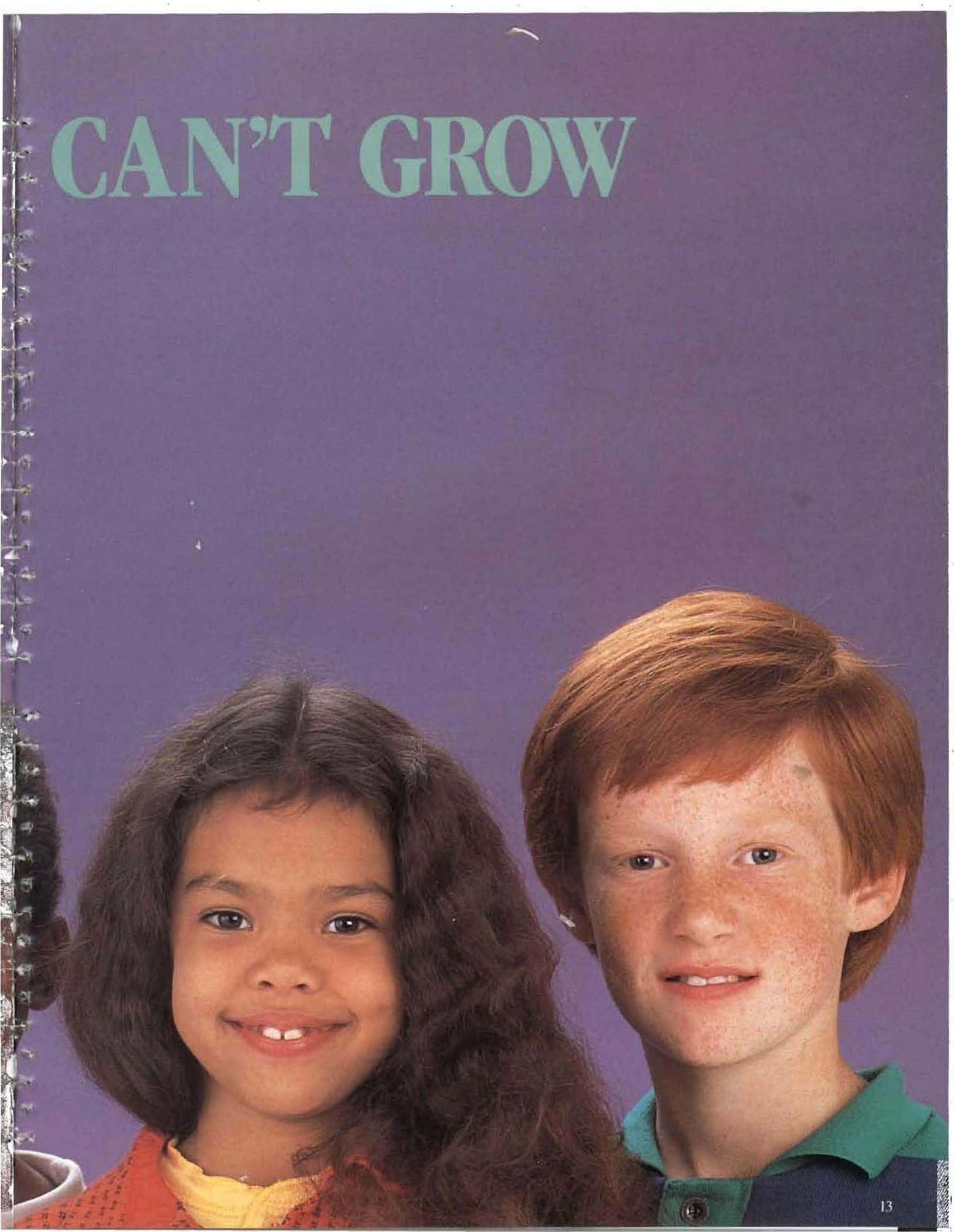
but Justin can

BY LINDA SAGE

Sitting on a stack of books to reach your desk isn't all there is to growing up short. When Justin Leib was in second grade and smaller than the smallest kindergartner, he had to put up with nicknames like "pee wee," "shrimp" and "munchkin." Wearing Levis like the other kids was out of the question because his sizes were emblazoned with Winnie-the-Pooh or Sesame Street characters. And instead of playing with other boys at recess, he was led around by older girls who wanted to mother this "blond and blue-eyed baby."



CAN'T GROW



Like many short children, Justin was average size at birth, weighing 7 pounds 8 ounces. Though he was a small toddler, that seemed quite normal because his mother is 5 feet 4 inches, and his father 5 feet 7 inches. Only when he reached the age of 4 did anyone notice a problem. Just before Justin entered kindergarten, the specialist who measured him for orthopedic shoes discovered that Justin's feet hadn't grown at all in the last year and a half.

About 2.5 percent of all children fall below the normal height range for their age — that's over 1.75 million kids in the United States alone. Those with abnormal proportions tend to have chromosomal defects or bone disorders, whereas children who are simply short may have kidney disease, gastrointestinal disorders or endocrine problems.

Short children like Justin, who have endocrine disorders, are the target of a new study at the School of Medicine that began last spring and will continue until 1990. Headed by Dennis Bier, M.D., professor of pediatrics and co-director of the Division of Endocrinology and Metabolism at Children's Hospital, the study aims to identify new causes of growth failure. It will also see which types of patients can respond to growth hormone, a protein that triggers growth.

Growth hormone has been used to treat short children for the past 25 years. The School of Medicine was one of the first institutions to use this therapy, but until recently the hormone had to be purified from the pea-sized pituitary glands of cadavers and was therefore in very short supply.

When Justin Leib sought treatment elsewhere in 1979, he was refused the hormone because he did not meet the strict criteria for its distribution. But on Washington's Birthday in 1983, he obtained treatment at Washington University by taking part in a clinical trial of human growth hormone made through recombinant DNA technology.

The recombinant hormone was approved by the FDA in October 1985, after the natural hormone was banned for further clinical use because in rare instances it seemed to be linked to a dementing neurological disease called Jakob-Creutzfeldt syndrome.

> "We have a lot of hypotheses, but we don't know whether individuals will respond unless we put our ideas into practice."

This normally rare condition is caused by a virus that infects the brain, so it could be transmitted by contaminated human pituitary tissue extracts.

When Justin started his growth hormone injections at the age of 8½, he was only 43½ inches tall — the height of an average 6-year-old. His response was immediate, and he began to grow an astonishing inch every two months as he started to catch up in height. "There was a time when he grew out of a pair of tennis shoes every six weeks," his mother recalls happily. "And last year, after we had a major fire at our house, we were given lots of gifts from friends. One was an expensive pair of jeans for Justin, which I saved for a trip to Disney World. But when we got there three weeks later, he couldn't get into them, and I had to go buy him another pair."

The boy who once heard his mother's friend describe him as "the little guy who's no bigger than a bar of soap" is now 58 inches tall — just over the average height for his 11½ years. When his family recently moved to a new town, and his mother Kathy had to explain why he was having shots, her new friends found it hard to believe that he had ever had a growth problem.

At present, the FDA sanctions growth hormone therapy only for children like Justin, with growth hormone deficiency. "But most of us feel that there are many other children who will respond to treatment, though this has not been clearly established," says William Daughaday, M.D., the Irene E. and Michael M. Karl Professor in Metabolism. "For example, there may be patients who are partially growth hormone deficient who may respond to higher doses than we were able to obtain in the past."

Widening the scope of growth hormone therapy isn't the only aim of the study; however, another goal is to identify defects other than growth hormone shortage that lead to short stature. "Five or six years ago, we realized that methods for evaluating growth deficiencies were not adequate," Bier says. "For example, many children that were diagnosed as growth-hormone deficient were not really lacking in the hormone. Instead, they were unable to release the hormone from the pituitary."

Only 10 percent of short children who come to the endocrine clinic because of their size have problems that can be routinely diagnosed. "The other 90 percent are the ones we are particularly interested in, regarding the mechanism of growth impairment," Daughaday says. "One of our major interests is in recognizing individuals who put out abnormal growth hormone or abnormal somatomedin, a growth-promoting protein that is made in the body in response to growth hormone."

The study will include about 50 of the 300 to 400 short children who are referred to Children's Hospital each year from southern Illinois and eastern Missouri. During a child's first visit, a team of pediatric endocrinologists consisting of Bier, Sherida Tollefsen, M.D., assistant professor of pediatrics, and David Dempsher, M.D., fellow in pediatric endocrinology, will take a medical history to screen out children who are not abnormally short, or whose growth deficiency is due to causes other than an endocrine disorder.

After screening, children who qualify for the study spend three days in Children's Hospital, where their ability to secrete growth hormone is measured with routine clinical tests. They also donate blood samples and a pinhead-sized patch of skin for new growth tests, which have been developed at Washington University. Over the next several weeks or months these samples are studied, and the children visit the hospital regularly to be accurately measured.

When the results of the tests are avail-

James Gavin III, M.D., uses radioimmunoassay techniques to determine individual patients' abilities to secrete growth hormone.

able, and growth rates are established, children come back to the hospital for another seven days. This time, rate of protein synthesis and breakdown is measured before and after a couple of days of growth hormone treatment. Since protein accretion is an essential component for the deposition of new tissues, these tests assess children's current capacity for growth.

Before leaving the hospital this second time, children begin thrice-weekly injections of growth hormone, which continue for six months — long enough to see even belated responses. If growth-rate increases by at least half an inch during this period, the child stays in the program and receives a further six months' supply of the hormone. Treating a 10- to 15-year-old child with growth hormone for one year costs $10,000 to $20,000, and that money comes from the $2-million grant awarded for the study by the National Institute of Child Health and Human Development.

Awareness that short stature can have many different causes came after scientists began to unravel the complex cascade of events that controls growth. When Daughaday came to the School of Medicine in the 1940s, it was thought that growth hormone acted directly on tissues to promote the synthesis of new materials, such as cartilage, that build the human body. So Daughaday tried to assay the hormone by determining in vitro its effect on the uptake of sulfate ions into cartilage — a measure of growth. Instead, he discovered that growth hormone has absolutely no effect on cartilage formation outside the human body.

By 1957, Daughaday discovered the reason for this anomaly. He found that serum from normal rats could stimulate sulfate intake, but the serum from rats whose pituitaries had been removed could not. This led him to the conclusion that serum normally contains a growth-promoting substance he called sulfation factor that is induced by growth hormone. This and other related proteins are now known as somatomedins becase they act as mediators between growth hormone and growing tissues.

The current hypothesis is that growth hormone does not directly stimulate growth, but rather acts through the intermediary protein somatomedin, which in turn triggers cells to increase their synthesis of proteins and other substances essential for growth. When growth hormone that has been released into the bloodstream by the pituitary reaches certain cells, it plugs into growth hormone receptors on their outer membranes, signaling them to produce somatomedin. This intermediary protein is released from these cells and binds to somatomedin receptors on other cells targeted for growth. The binding of somatomedin to these cells stimulates them to produce proteins and other substances essential for growth.

This dual-control system, involving both growth hormone and somatomedin, seems to have many advantages over a system involving growth hormone alone, but it also provides more scope for error. Thus short stature could theoretically be due not only to errors in the production or secretion of growth hormone, but also to the synthesis of a biologically inactive growth hormone that can't bind to growth hormone receptors. Deficiencies or defects in those receptors or in somatomedin could also stunt growth, as could too few or defective somatomedin receptors.

These hypotheses evolved from studies with animals and cultured human cell lines. The Washington University study will see how they hold up during clinical testing, when defects identified in children by laboratory tests will be correlated with response — or lack of response — to therapy. For example, a child with defective somatomedin shouldn't respond to growth hormone if control of growth has been interpreted correctly.

"We have a lot of hypotheses," Daughaday says, "but we don't know whether individuals will respond unless we put our tests into practice. We need to know if our criteria for predicting a growth defect are accurate enough."

The unique aspect of this study is that it brings together five principal investigators whose combined research covers every link in the chain of events between growth hormone secretion from the pituitary and protein synthesis in tissues.

James Gavin III, M.D., associate professor of medicine, focuses on the events between growth hormone secretion and somatomedin synthesis. He measures the amount of growth hormone a child can secrete by adding a sample of the child's serum to radioactive growth hormone combined with an antibody. Since each antibody molecule can combine with only one growth hormone molecule, some of the

radiolabeled molecules are displaced if there is growth hormone in the serum. The concentration of the latter can be calculated from the amount of radioactivity that remains bound. The principle is similar to a game of musical chairs. If five people are playing the game with five chairs, each will be able to sit down. But if an extra 20 people suddenly gatecrash the party, the chance of one of the original players getting a chair falls to one in five. One could calculate the number of gatecrashers from the number of original guests that manage to sit down.

Although this standard radioimmunoassay measures the quantity of growth hormone, it reveals nothing about its biological activity because the part of the growth hormone molecule that binds to an antibody is different from the part that binds to the growth hormone receptor. Yet Gavin has learned how to use the same principle to assay biological activity, using different "players" and different "chairs" with a cultured human cell line as a source of growth hormone that can compete with radioactive growth hormone already bound to the cell surface. If the growth hormone in the serum cannot bind to the receptors, Gavin deduces that it has an abnormal structure.

To assay the receptor itself, Gavin hopes to compare the binding of radioactive growth hormone to fibroblasts from a cell bank with tha. to fibroblasts grown from skin samples of the short children in the study. So far, he has perfected the technique for animal cells, and within the next few months he hopes to determine the optimal conditions for measuring human growth hormone receptors.

The next link in the chain is somatomedin synthesis, for this protein is the net result of the binding of growth hormone to its receptor. After incubating a child's fibroblasts with growth hormone, Gavin measures the quantity and activity of the resulting somatomedin with a radioimmunoassay and a biological assay.

The Washington University team is also studying somatomedin synthesis at its most basic level — by looking at the gene that codes for the protein. Peter Rotwein, M.D., assistant professor of medicine, finished sequencing the normal somatomedin gene last year. Now he will look at the gene in children with seemingly abnormal somatomedin, obtaining the necessary DNA from their white blood cells. "The assay of somatomedin per se is step one — kind of a best guess that this one might be abnormal," he says. "So we are going to take it from there and try to confirm that the protein is coded for by an abnormal gene. Then we'll try to show that the abnormal gene is the problem in that particular individual's failure to grow."

When Justin started his growth hormone injections at the age of 8½, he was only 43½ inches tall — the height of an average 6-year-old.

Rotwein will also alter the gene in cultured cells and look at the effect on somatomedin production and activity. He hopes to study the regulation of somatomedin synthesis as well, asking how the binding of growth hormone to its receptor switches on somatomedin production.

The final link in the chain — the somatomedin receptor — is assayed in animal cells by Gavin in much the same way as the growth hormone receptor, but with radiolabeled somatomedin in place of growth hormone. Using an alternative approach in human cells, Daughaday measures the uptake of radioactive amino acid analogs into fibroblasts that he stimulates with commercial somatomedin. Since amino acid uptake is one of several events that somatomedin binding switches on, its rate reflects the number of receptors on the cell surface and important post-receptor mechanisms related to cell growth.

Tollefsen studies the structure and synthesis of the somatomedin receptor, trying to develop methods that eventually will pinpoint precise defects. She just achieved the first purification of the receptor, which consists of four polypeptide subunits — two alpha and two beta — plus an undetermined number of side chains built of sugars. Tollefsen's current goal is to study the biosynthesis of the receptor in cultured fibroblasts, looking at the complex processing of its precursors. Once she has uncovered the normal sequence of events, she will look for abnormalities in children with short stature.

The study of protein synthesis — the business end of the growth process — is the province of Bier and Dempsher, and is a natural outcome of Bier's 13-year interest in the effects of hormones, nutrition and disease on human metabolism. As no single test can tell if a child's protein metabolism is normal, the researchers do several assays. On the one hand, they look at the incorporation of amino acids from food into proteins in the bloodstream. On the other hand, they measure the wastage of these amino acids as their atoms are excreted in carbon dioxide in breath and urea in urine. The radioactive labels that are used in the laboratory tests would be harmful to children, so they label the amino acids with harmless stable isotopes that can be detected by their slightly different mass.

By bringing together this wide range of expertise in clinical medicine and basic biology, the researchers aim to diagnose any defect in the growth-controlling sequence. Such a study is essential to further progress, for physicians must be able to detect the cause of a growth deficiency before they can plan rational therapy. The researchers are hopeful their labors will open the way to new treatments, such as injections with recombinant somatomedin for children with defective growth hormone receptors or somatomedin genes. Then, like Justin Leib, more children will be able to outgrow their growth deficiencies. ■

"If this were any other virus, this would be the perfect vaccine. It replicates, but doesn't kill. It's an attenuated virus just like everyone gets vaccinated with for polio."

AIDS Against Itself

BY KATHY WILL

By slicing into the DNA of the HTLV-III virus, Lee Ratner has created two mutants that do not kill human immune cells, but may serve as weapons against the original form.

Like a night watchman on his appointed rounds, an ever-vigilant helper T cell patrols a vessel of the lower genital tract.

This circulating sentinel detects a foreign antigen in a nearby capillary bed, determining the invader to be a white blood cell of similar cell type. But as the two T cells meet, the AIDS virus that was hiding in the invading cell slips through the cell membranes into the defending cell before that cell can sound the alarm.

Once inside the inactive helper T cell, the subversive AIDS virus decodes genetic information from its RNA core into a DNA form that is recognized by the T cell as its own and inserted into its chromosomes. There it may lie dormant for weeks, months, even years until some other infection triggers the invaded cell to divide. The viral DNA then reprograms a key component of the T cell's genetic machinery, so that the cell churns out copies of the virus faster than it can manufacture its own cell parts.

One by one, these viral clones bud from the cell to infect neighboring T cells. And after enough copies of the virus have been produced, the ungrateful AIDS virus kills its host cell. By killing these critical lymphocytes, the AIDS virus short-circuits the entire immune system. Without enough helper T cells to signal the attack, the other soldiers of the immune system — phagocytes, killer cells and B cells — are never called into action, leaving the body wide open to a constant assault of secondary infections that include cancer, herpes, inflammations of the lung and brain, fungal infections and prolonged diarrhea.

The human immune system is no match for the rapidly spreading AIDS virus, as evidenced by the fact that half of the more than 23,000 Americans who have been diagnosed with AIDS are already dead. But while the AIDS virus easily defeats the body's first line of defense (the immune system), this virus has yet to receive the brunt of humanity's surest defense — the mind.

Taking the lead in the mind's war on the microbe is Lee Ratner, M.D., Ph.D., assistant professor of medicine. Collaborating with Robert C. Gallo, M.D., from the National Cancer Institute and six other re-

"The problem with this class of viruses is that they get converted into DNA forms, which go into your chromosomes and stay there forever."

Lee Ratner, M.D., Ph.D.

searchers, Ratner has successfully cloned two mutants of the AIDS virus that may eventually be used to beat the original form at its own game.

The genetically altered viruses behave in exactly the same way as the original AIDS virus, except that they do not kill T cells. Ratner and his colleagues, who recently reported their unprecedented results in an August 8 issue of *Science,* created disarmed variants of the AIDS virus by slicing into its genes.

Ratner and his fellow investigators opened up circular strands of the virus' DNA with a bacterial enzyme that cuts through the DNA at only one point on the circle. Then they added a second enzyme that chews inwards from both ends of the DNA, as if it were removing beads from the ends of an unclapsed necklace. In this way, they created holes of varying size along the DNA strand. After ligating or "reclapsing" the ends, the investigators isolated six genetic variants which, when added to cultured T cells, produced six correspondingly mutated viruses.

The two non-lethal mutants were created more or less by accident, according to Ratner. They were formed when the enzyme chewed past the suspected killing gene into the next gene, which really does control cell killing. The four mutants that contained alterations only in the originally suspected killing gene retained their ability to kill, ruling out that gene as the killing gene.

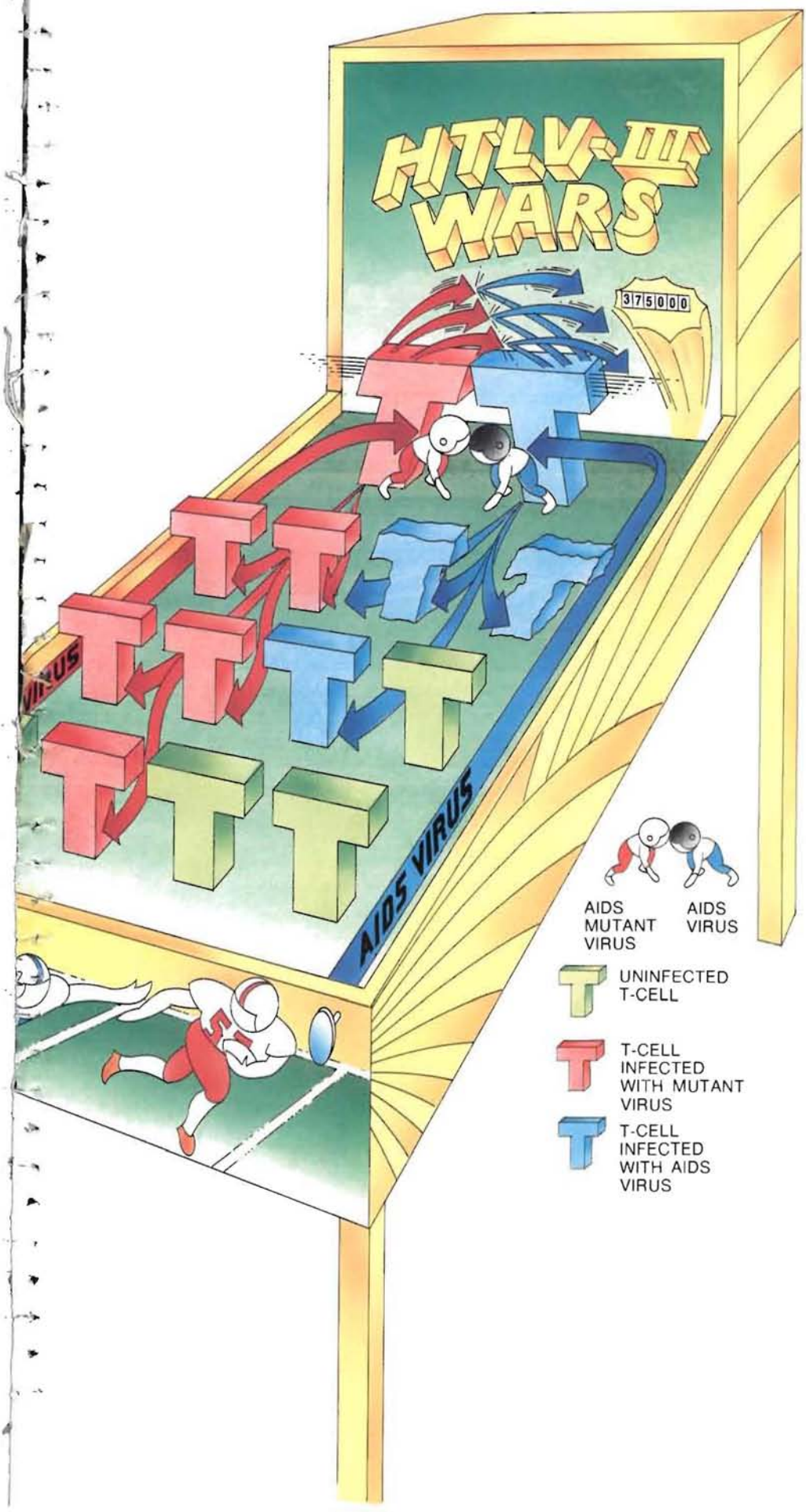
Because non-lethal mutants of the AIDS virus replicate just like the killing form, they may eventually be used to treat AIDS patients in the hope that the non-lethal forms might outcompete the killing variety for helper T cells. Studies are already underway to determine whether or not these mutants can outcompete the killing virus in cultured T cells. "If this were any other virus, this would be the perfect vaccine," Ratner says. "It replicates, but doesn't kill. It's an attenuated virus just like everyone gets vaccinated with for polio."

Although mutants of the virus may be used to help people who already have AIDS, they will probably never be used as a vaccine for non-infected patients. "The problem with this class of viruses is that they get converted into DNA forms, which go into your chromosomes and stay there forever," Ratner says. A live retrovirus will probably never be of any use as a vaccine, because it could damage normal genes. "Whether it actually would or not, we don't know," Ratner says. "But it's too dangerous to take a chance."

Even more important than any clinical role they may play, Ratner's mutants have provided AIDS researchers with a powerful new tool for learning exactly how the AIDS virus kills the T cell.

"What we have is a mutant virus and a wild type virus — both of which grow well — and yet one kills, and one doesn't. Now we'll be able to separate out the effects of

Dr. Ratner's AIDS virus mutants invade T cells in much the same way as the original virus. Unlike the original, however, the mutants are not lethal to T cells. Cells already occupied by mutant forms may be protected from subsequent infection by the deadly variety.



virus replication alone from that of cell killing, by comparing the effects of our killing-variety virus to our now-mutant virus," Ratner says.

More specifically, Ratner and his colleagues are using the mutant virus/killing virus comparison to look for cellular proteins that might be involved in cell killing. "There are a number of proteins — some that we know about and probably some that we don't know about — that are made by lymphocytes and kill lymphocytes," Ratner says.

Ratner speculates that if researchers could identify such a cellular protein, they would eventually be able to engineer a drug that interferes with the production of that protein. "Our major goal is not to sort through the chemistry shelf for drugs that inhibit viral replication," he says. "Rather, by learning what structures are involved in killing lymphocytes, we'll have a way to actually design drugs based on those structures."

A former research fellow under Gallo at the NCI, Ratner has made several substantial contributions to frontline AIDS research. He was one of 19 individuals responsible for initially cracking the virus' genetic code, and one of the first researchers to produce its biologically active molecular clone.

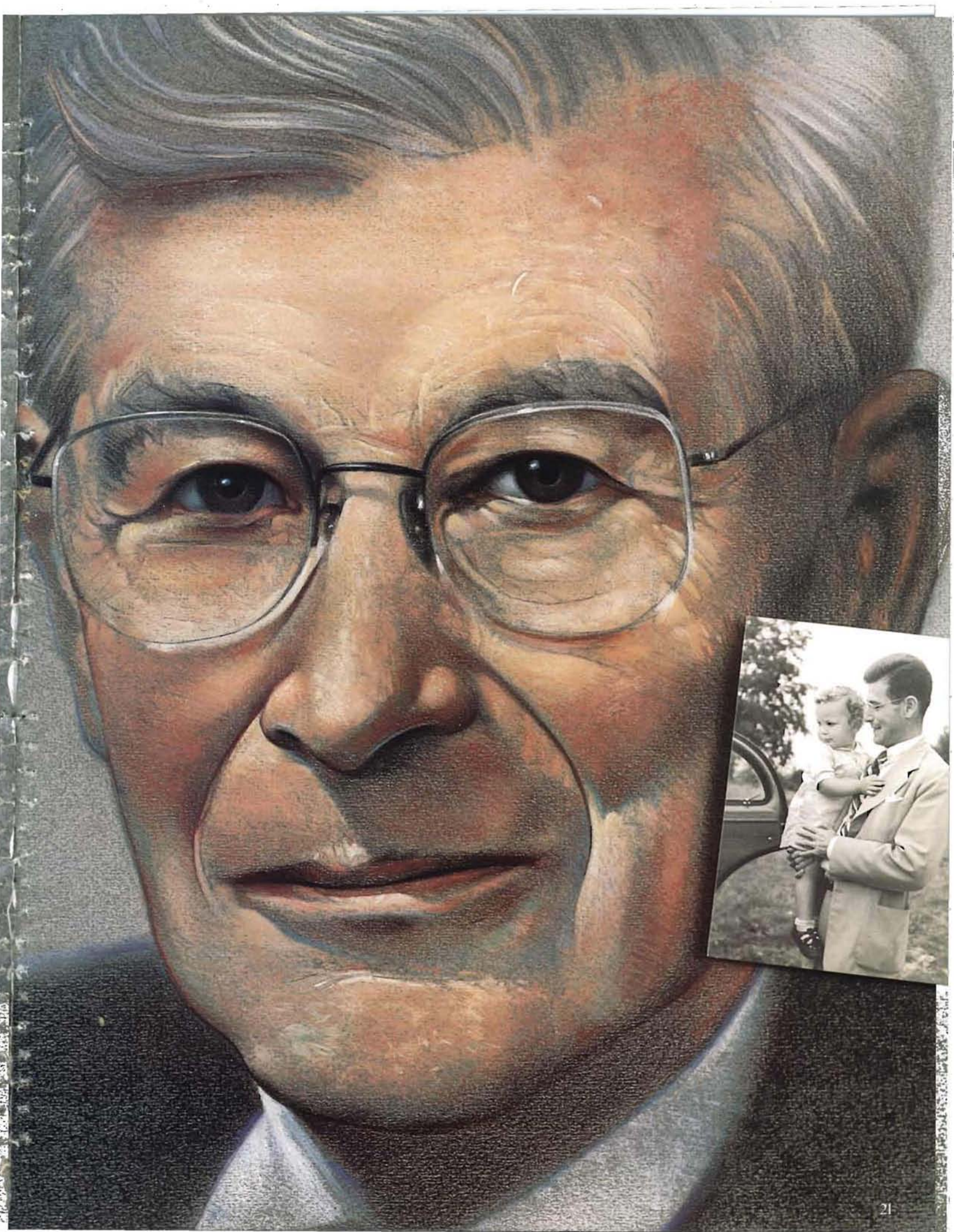
Although he works so closely with the virus, Ratner is not worried about catching AIDS. "All of the evidence suggests that the way we work with the virus is very safe," he says. "Nobody who's ever worked in an AIDS research lab has ever developed antibodies to the virus."

In the long run, man's battle with AIDS may actually serve to sharpen his mind for the larger war against all microbes. "I think we're going to get a lot of information about virology in general from this, because there's never been this kind of intense research on one virus," Ratner says. "More has been done in the last two years on this virus than has been done in the last 40 years on the polio virus. By studying one virus extremely intensely, we're actually learning more about the basic biology of all viruses." ■

Henry Schwartz's Constellation Of Fortuitous Events

BY DEBRA BERNARDO

In 1936, a young physician relinquished his junior faculty position at Harvard and traveled to St. Louis to train for one year in neurosurgery. The move, as it turned out, ended a personal tug-of-war for Henry Gerard Schwartz, M.D., who had been so intensely interested in the anatomy of the nervous system that he had briefly forsaken his chosen field of neurosurgery for basic science research.



His decision to resume his career in surgery led him in 1936 to Washington University School of Medicine, where he was appointed a fellow in neurosurgery under Ernest Sachs, M.D., who was chief of the neurosurgical service and held the first academic appointment as professor of neurosurgery in the United States.

Woodstock, Vermont, 1935

Although his original intention was to stay just one year, 50 years later Schwartz is still here.

Schwartz's career at the School of Medicine has been a distinguished one. The long-time head of the Department of Neurological Surgery, now August A. Busch Professor Emeritus, is one of the most esteemed neurosurgeons in the world. He has received every major honor from his colleagues, who recognize him for his scholar's mind, his numerous clinical contributions and advances and particularly for building one of the great neurosurgery training programs: 14 of the 45 residents Schwartz trained in his 28 years as department head have gone on to direct their own training programs.

Henry and Edith, 1945

From his residents, he demanded excellence. The almost impossibly high standards he set for them, however, were no higher than those he set for himself. Colleagues and former residents alike describe him as a dedicated physician and perfectionist in patient care.

"In his work habits, his day-to-day activity, there is a painful attention to detail and an integrity that characterizes his practice of medicine and his way of life," comments Sidney Goldring, M.D., who trained under Schwartz in the early 1950s and succeeded him as professor and head of the Department of Neurological Surgery.

Goldring has written of Schwartz, "He demanded excellence from his men, and the rigors encountered by his residents in meeting those demands have become legendary."

Schwartz describes himself as a "tough taskmaster." Of his trainees he says, chuckling, "They'll probably call me all kinds of names and then they'll probably say that they love me as much as I love them."

Robert King, M.D., one of Schwartz's first residents, laughingly admits that some people would describe Schwartz as "more than tough. But there was never any question that his concern was for your own development and for the patient's good. And he was fair," King adds. After completing his residency, King went on to become Schwartz's first faculty appointee, leaving the medical center in 1957 to become head of the neurosurgery program at Syracuse University. "The likelihood is that I've translated into our program and into my own life many things from him that I don't link directly back to him. His indirect persuasions can be very, very powerful."

In a 1974 address to the Congress of Neurological Surgeons, Schwartz spoke of his almost paternal feelings toward his trainees, quoting a colleague's words about family: " 'It is with our children that we have the unusual opportunity to help them attain responsible adulthood and take their active place in society. . . . They should know our love where love is not indulgence and giving in, but is to a great degree discipline, where we care enough to want them to grow up right.' "

He continued, "Better than any phrase I might devise, this expresses my own feeling toward those young men whom good fortune has sent to my program. I have demanded much of them but have wanted much for them. Their successes have been my reward and my job."

Residency under Schwartz *was* difficult, recalls William F. Collins, M.D., who also trained with him in the early 1950s and now heads the department of surgery at Yale University Medical Center.

"I got so upset when he was upset with me one time, I told him . . . that I not only didn't have to be a neurosurgeon, I didn't even have to be a doctor. I could be something else if he thought I was that bad, but I wanted another opinion," Collins recounts. "His reply to me was, 'Don't be foolish. I'll tell you when you're not good enough to go on,' and he walked off. That," he laughs, "was a compliment."

Today, Collins considers Schwartz a close personal and professional friend. "He has been probably more supportive of me than almost anybody I know and has helped tremendously to allow me to develop the two programs that I've set up." According to Collins, one of Schwartz's very striking traits is his generosity in helping his former residents iron out their prob-

lems, develop programs and decide which direction to go in the profession.

Goldring agrees. "He puts a tremendous amount of emphasis on loyalty and is extremely loyal to those he respects and works with."

Schwartz's neurosurgery training program's success, many say, is due in large part to his emphasis on research. The residency program he set up in 1946 was one of the first in the country to set aside a substantial block of time solely for research. Neurosurgeons trained by Schwartz, therefore, had an attribute that most other residents lacked — a background in either basic or clinical research on the nervous system.

As Collins points out, "They not only had a very careful instruction in surgery — to the point that it was almost impossible to please him completely — but at the same time, a very thorough instruction in basic anatomy and basic pathology and then an opportunity to use investigative techniques to study the nervous system. That combination was extremely rare in any of the neurosurgical programs at that time."

"He set extremely high standards for people going through that program, so that he required not only to know what you should do, but why you should do it. And that . . . was a change . . . recognized throughout the country, so that the major training programs really started to follow his lead.

"He really was the pivotal point as to the change that occurred from developing a person who was a technical surgeon to one who was an academic neurosurgeon."

Schwartz himself takes a modest view. The values that he tried to instill in his residents, he says, were those of the greats of medicine: William Halsted, the Johns Hopkins surgeon who trained numerous physicians and whose philosophy dominates the profession even today; Evarts Graham, head of surgery at Washington University and his very close friend; another good friend, Edwin Churchill, professor of surgery at Harvard; and many others from the rosters of medical history.

"They all had the concept of providing for their trainees the facilities and the atmosphere to think for themselves, to discipline themselves as far as hard work and the care of the patient was concerned and to push the frontiers forward and learn more about the field in which they were working," Schwartz says.

"And to do that, they made it possible for their men to learn the techniques as well as the art of medicine — of surgery — and the ability to seek out answers, both in the clinic and in the laboratory. And all of these wonderful individuals — almost all of them — had somewhere along the line taken the time to pursue basic scientific work."

Most of the great contributors to surgery and neurosurgery, Schwartz knew personally. His life, he says, has been "a constellation of fortuitous events."

"Environment, luck — good or bad — and fortuitous events make us what we are," says the man who in 1924, at the age of 15, entered Princeton University knowing that he wished to become a neurosurgeon. It was at Princeton that Schwartz conducted his first brain surgery on the earthworm, "the lowliest creature."

Because of its ability to regenerate itself, the earthworm was an ideal subject for Schwartz, who was interested in learning the process involved in regeneration. He began to study its nervous system, removing the main cerebral ganglia, the nerve centers. "I became fairly adept at removing these ganglia and then watching them grow back," he recollects.

Schwartz continued this research at Johns Hopkins School of Medicine, where he enrolled after receiving his bachelor of arts degree in 1928. There, he worked with anatomy professor Marian Hines.

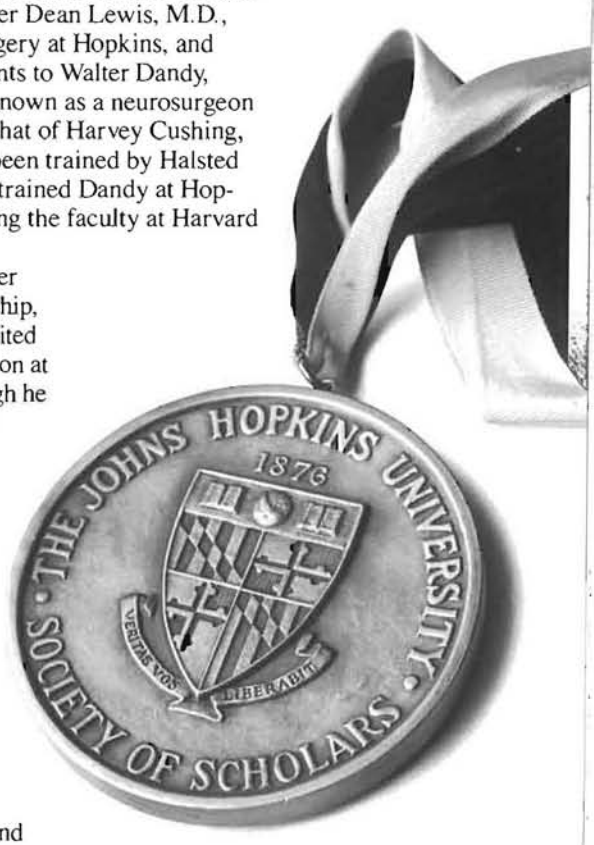
"She was certainly my guiding light," he says. "She had heard that I had done this work at Princeton and she asked me about it. She thought I ought to continue it. That began a lifelong relationship. She was a superb woman, one of the finest women in the world."

Hines — as well as other prominent anatomists and biologists at Hopkins — greatly influenced Schwartz, who during that period realized his lifelong interest in anatomy and the nervous system. At the same time, he was inspired by clinicians; some of the greats of surgery and neurosurgery worked at Hopkins in those days.

After receiving his Doctor of Medicine degree in 1932, Schwartz interned in general surgery under Dean Lewis, M.D., then head of surgery at Hopkins, and passed instruments to Walter Dandy, M.D. Dandy's renown as a neurosurgeon at least equaled that of Harvey Cushing, M.D., who had been trained by Halsted and who in turn trained Dandy at Hopkins before joining the faculty at Harvard University.

During the latter part of his internship, Schwartz was invited by Dandy to stay on at Hopkins. Although he was intrigued by neurosurgery, Schwartz opted instead to pursue anatomy and neuroanatomy as a National Research Council Fellow at Harvard.

The one-year fellowship stretched to two, and Schwartz found



Current River, Mo, 1961

himself with "one foot in both camps, anatomy and neurosurgery." At that point he was "still waivering" and received a position as instructor in anatomy at Harvard.

It was in Boston that Schwartz and his "very attractive, very bright" medical school classmate, Edith Courtenay ("Reedie") Robinson, were able to marry. Back then it was "very rare, almost unheard of," for a medical student or resident to marry. But for Schwartz, marriage to Reedie was clearly the most fortuitous of events.

"She is the most fortunate thing that ever happened to me," he says. "From her, I subsequently realized how vital it is . . . to have a wife who can not only speak the same language, but more important, can understand and sympathize, worry, cheer you up . . . and help you to maintain your own sanity and a certain amount of equanimity.

"She has equanimity in tremendous amounts and has been a tremendous factor in everything I've done." Edith Robinson, M.D., is a clinical assistant professor emeritus of pediatrics at the School of Medicine.

Of the stint at Harvard, Schwartz has said, "Those were three very good years . . . indeed a happy time." He decided, however, to return to clinical work, and that was how Schwartz ended up as Sachs' fellow at Washington University.

Those were the formative days of neurosurgery at Washington University School of Medicine and elsewhere. The St. Louis program, like all neurosurgery programs then, was not formalized. The first specialty board, the American Board of Neurosurgery, and specific requirements for certification were established during World War II.

"Until then, the requirements were very vague," Schwartz explains. "If the chief of the service that you'd been working on said you were okay to take the boards, well, that was all that was needed."

At Washington University, the Schwartz's came into daily contact with people who since have become institutional cornerstones: Phillip Shaffer, Carl and Gertrude Cori, Joe Erlanger, George Bishop, Evarts Graham, James O'Leary and many others. These early contacts, which developed into warm friendships, were possible because the school was smaller then, Schwartz comments.

"In St. Louis in those days . . . it was easy to get to know other individuals in other departments on both sides of the street, the pre-clinical side and the clinical side . . . The competition along with camaraderie was there; likes and dislikes were manifest. But nevertheless, it was relatively easy to get to know people and to exchange ideas."

In particular Schwartz remembers luncheon discussions in which faculty from both sides of the street would eat lunch together and talk about their experiments.

Schwartz found time for those lunches, but it wasn't easy with the work load he had under Sachs, "an extremely tough taskmaster. There were no nights off, there were no weekends off, there were no days off. You were expected to meet the professor at 6 or 6:30 in the morning and then make a quick round before going into the operating room. We did all the x-rays ourselves — the air injections, positioning the patients and so on — things that we don't do anymore.

"After operating, Dr. Sachs would usually go to his office downtown at the University Club building, or he'd stop at the lab office across the street and dictate his notes and then go downtown. Meanwhile, we made rounds and took care of the chores. When he'd come back in the late afternoon, at 5:30 or 6, we'd make rounds again. And if there were new patients who had come in, we'd have to work them up and dictate the notes, write the orders and then start all over again. That was just the way it was."

At the time, the only neurosurgery lab was a pathology lab that Sachs supported with his own funds. Although Sachs would have preferred Schwartz to help section and examine tumors in the neuropathology lab, Schwartz gravitated to the lab of neurophysiologist George Bishop.

"Those of us who were interested in neurophysiology and that kind of research worked with Bishop in his lab on the eighth floor of McMillan," he remembers. "We worked up there on all our experimental work daily, by his good grace, really.

"We were all relatively young. Of course, Dr. Bishop was many stages beyond us, but he was very, very happy to have people working with him. He was a tough investigator, but a damn good one, and a superb mentor. We were very lucky."

Over the years, Schwartz's projects yielded a number of significant advances. With another fellow, Alan Kerr, he achieved the first direct recording of electrical activity from the exposed human brain in the United States. Using a cathode ray oscilloscope that Schwartz built and silver ball electrodes, they were able to record this activity in the brief five minutes Sachs allowed them.

"It was so amateurish it's laughable, when I think back," he says, "compared to just a few years later, and particularly now. But back then, five minutes was pretty generous because Dr. Sachs was worried and so were we. His feeling was 'You're wasting time here. You have the patient's brain exposed and you'd better be doing something for the patient instead of fooling around with this business.' "

Later, when Schwartz was at City Hospital, he conducted one of the first randomized studies in neurological surgery on the effect of lumbar puncture in reducing intracranial pressure in severe head injuries. "There was a question whether every patient with a head injury should have a lumbar puncture . . . Some people thought it would be dangerous, actually, if there was too much pressure up above, so that was why we ran this series." The study concluded that those cases could be handled without repeated spinal punctures.

Also at City Hospital, Schwartz developed medullary tractotomy, an operation for intractable, or unrelieved, pain. The operation involves putting a lesion in the medulla, a part of the brain stem, to interrupt pain pathways and relieve severe facial pain. Though it's no longer necessary, at the time it was "a pretty good operation, and it helped to elucidate some of the anatomy" of pain paths through the brain stem.

After World War II, he became enchanted with cervical cordotomy, which he also developed, to abolish intractable pain at a high cervical level. The procedure eliminates pain in the lower extremities, by operating in the neck rather than the brain stem.

"War is a breeding ground for surgeons," Schwartz has said. "Whether we like it or not, we have to admit that for surgeons the experience — the treatment of wounds, treatment of infection, the basic things one could learn about the physiology of the engine, the physiology of various organs — this is an experience which I think should not be overlooked. Not that I advocate war as a part of training. It's a disastrous situation. But nevertheless, the experiences gained in war can be put to good use."

In 1941, Schwartz joined the medical unit affiliated with Washington University and Barnes Hospital as assistant chief of the surgical service. He was fortunate in his assignments, he says, because they allowed him to learn and to contribute to the knowledge of neurosurgical handling of wounds to the head and nerves.

In Africa, he encountered trying times. His equipment had been sunk, making it, of course, difficult to operate. Yet he managed.

"We stole some equipment," he laughs. "Until we got that, I carried a curette and a rongeur my wife sent me. And we had a bayonet forceps, but we did not have a cautery; we did not have clips. We had a drill that we stole. In most cases, the skull was already partially open from the wound, and then with a rongeur you could enlarge the hole."

The hot cautery they devised is "incredible in this day and age. We used an alcohol lamp next to the operating table and when we got a bleeder that was too small to tie off, well we'd use the forceps — turn around, heat the bayonet until it got hot and then touch the bleeder."

Despite the hardships in Africa, Schwartz made significant contributions and, in fact, was responsible for changing military procedure on how to treat injuries to the head and nerves. Policy had been to leave contaminated head wounds open to drain. That led, however, to increased infections, herniations of the brain and a high mortality rate. Schwartz and his team learned that the death rate could be tremendously reduced by cleaning wounds thoroughly and using precise surgery.

The same held true for nerve injuries. Under Schwartz, the policy was to debride nerve wounds, permit them to heal and then three to four weeks later operate on the nerve. That approach bettered soldiers' chances of recovering function.

"There were contaminated wounds, you see, because in the African campaign evacuation was so bad we'd get patients up to several days after they'd been wounded before anything was done for them. And here were dirty, contaminated wounds that ordinarily we would have just cleaned up a little and left open to drain. But we found it

Fort Benning, Georgia, 1942

Dr. Sachs' summer home in Keen Valley, New York, 1937.

was best to operate on them, cut out all the damaged tissue and then close them up. So that became the general policy in Africa."

After Africa, Schwartz served in Algiers, Italy and France. Just before his discharge, he completed a brief stint as chief of neurological surgery at Kennedy General Hospital in Memphis in 1945. That year he was awarded the military's prestigious Legion of Merit, and in 1946 returned to Washington University, where Evarts Graham named him professor and head of neurological surgery.

This, Goldring has said, began the phase of his life when most of American medicine believes Schwartz made his greatest contribution, training neurosurgeons. Goldring, in writing about Schwartz, has noted, "he has always de-emphasized the role of the teacher, arguing that it is of first importance to 'pick a good man; thereafter he learns, you don't teach him.' I . . . believe that in his modesty he tells but half the story. Equally important is the fact that the program director cares."

Although his residency training program was Schwartz's most consuming interest as department head, he has served steadily as a neurosurgical consultant to the Army and the Veterans Administration. His most active period as a consultant was during the late 1960s when, as neurosurgical consultant to the Surgeon General, he traveled to Vietnam to observe neurosurgery in the field.

Also, from 1965–67 he took on the position of acting head of the Department of Surgery and acting surgeon-in-chief at Barnes Hospital in addition to his responsibilities as neurosurgery head and neurosurgeon-in-chief at Barnes, Children's and Jewish hospitals.

In 1970, he was named the August A. Busch Jr. Professor of Neurological Surgery and four years later stepped down as head of the department. Rather than slacken his pace, Schwartz chose to use his extra time to begin new projects.

He became editor of the prestigious *Journal of Neurosurgery* in 1975, ostensibly for three years. Nine years later, the job — a demanding one — was turned over to his former student, Collins.

Schwartz also was instrumental in establishing the craniofacial reconstruction program at the medical center in 1978. According to the program director Jeffrey Marsh, M.D., "If it had not been for him and his willingness to not only lend his intellectual and spiritual support, but to be physically involved as the neurosurgeon and to spend many long hours doing that — sort of developing a whole new career at the end of his career — I think we would have had great trouble getting off the ground."

Schwartz himself says he became "enamored" with craniofacial work, much preferring it to "ordinary tumors." He stopped serving as neurosurgeon for the craniofacial cases about two years ago, but remains interested. To this day, Marsh points out, Schwartz sends him articles related to craniofacial reconstruction and follows up on favorite patients when they come in for checkups.

Schwartz's latest project is the Vietnam Head Injury study, the most comprehensive study ever conducted of penetrating head injuries. He is one of five members of a directorate that oversees this Department of Defense study.

The ongoing study, which began in 1981, compares 520 brain-injured veterans to 85 uninjured veterans. Data collected from the study have demonstrated improved neurosurgical and neurological management of brain injuries and illustrated how brain injuries affect thinking, memory and mood. Researchers are now analyzing data for insights into cognitive disability, social adjustment, mood, intelligence and other psychometric variables.

Schwartz has received virtually every honor in neurosurgery, including the Distinguished Service Award from both the American Board of Neurological Surgery and the Society of Neurosurgeons, the Harvey Cushing Medal from the American Association of Neurological Surgeons and election in 1985 as honorary president of the World Federation of Neurosurgical Societies. He is a member of the Johns Hopkins Society of Scholars and is profiled in "Leaders in American Medicine," a videotape made for the AOA National Library of Medicine.

He has held many appointments, among them chairmanship of the American Board of Neurological Surgery, presidency of all the major neurosurgical societies, and vice presidency of the American College of Surgeons and the American Surgical Association. In 1983, his colleagues and former residents established the Henry G. Schwartz Lectureship, now delivered annually at the School of Medicine.

"As of July 1, I completely quit operating," Schwartz says. He is a familiar sight in the halls, with his distinguished white hair, tall spare frame and a walk that he sort of leans into, as though he's impatient to get to his destination. His interest, he chuckles, is "surviving — surviving day to day." But, he adds, "I still do a little work around here." ■

Alumni Usher in New Loan Program

Twenty-five students and their benefactors ushered in the new Medical Scholars Loan Program by wining and dining together this past September at St. Louis' Racquet Club East.

The program was established last year in an effort to help students meet the high cost of medical education with interest-free loans, thereby upholding the long-standing principle that no student should have to forgo medical education at Washington University because of financial duress. Alumni and friends contributed a total of more than $36,000 to the program, which was matched by the Washington University Medical Center Alumni Association to establish 25 interest-free student loans.

Summing up donor sentiments, Henry G. Schwartz, M.D., August A. Busch Professor Emeritus of Neurosurgery, explained his reason for establishing one of 11 named loans: "These students need money to help them get through school; they're all broke. It's important for us to make it possible for good candidates to come here and stay here."

The Alumni Association's Executive Council, which met prior to the cocktail reception and dinner, announced its intention to do just that — by matching this year's coming donations to the program up to $50,000. Presenting a check for $36,914 to Samuel B. Guze, M.D., vice chancellor for medical affairs, Donald G. Sessions, M.D. '62, president of the Alumni Association, described his group's contribution as "a gift that can only match the interest and concern of alumni towards their medical school."

Top: Washington University fashion design students entertain spouses during the Executive Council meeting. Center: Tara Ann Rumbarger and her donor, Mitchell Yanow, enjoy dinner at the Racquet Club East. Bottom: Marvin E. Levin and senior student, Robert W. Tolan, enjoy each other's company at the Medical Scholars Loan Program Dinner.

In addition to formal recognition, the evening's events provided donors and students a more informal chance to meet. Those students who received named loans welcomed the special opportunity to meet and thank their donors one-on-one.

Named loans established under the program were made possible by the Dr. Joe M. Boyles Memorial Loan Fund, established by Mrs. Joe M. Boyles; the Dr. and Mrs. Robert C. Drews Loan Fund; the Dr. and Mrs. Marvin E. Levin Loan Fund; the Loan fund in honor of Dr. Eli Robins and Dr. Samuel Guze, established by Dr. Thomas F. Richardson; the Dr. and Mrs. Henry G. Schwartz Loan Fund; the Dr. and Mrs. William L. Topp Loan Fund; the Dr. and Mrs. Mitchell Yanow Loan Fund; and the Washington University Medical Center Alumni Association Loan Fund.

Annual programs chairman Robert C. Drews, M.D., who spearheaded the loan program funding, concluded the short program that followed dinner by wishing the students the best for the future and assuring guests that the students "can be confident that they are achieving the best. Washington University is one of the best because it has one of the best student bodies." ■

Free-interest loans aid seniors through final year

"The most important thing is not to get bored with your job," Barbara M. Scavone, M.D. '87, says of medicine and of life in general. "No matter how much work you have or how little sleep you get, you have to look at it as fun, or you'll never survive," she says.

Taking time to relax and pursue outside interests off the job is one way to avoid boredom on the job, according to the School of Medicine senior from Glen Ellyn, Illinois. "If you live, drink and eat medicine, you're going to burn out," she remarks. "I find that I'm much more enthusiastic about my work when I put aside an hour or two each day to sew or read a good book."

"The fact that alumni have donated money to help us out has really boosted student morale."

Finding the time and place for her favorite extracurricular activity — the piano — is difficult at times, but she practices at the student dormitory, Olin Hall, whenever she can. "The piano's not exactly the type of instrument you can carry around with you," she says. "I really enjoy sitting down at my mom's piano when I'm home." Scavone has been hammering ivory since the age of six, but her musical talents are by no means locked to the keyboard. She sings in her mother's church choir on Christmas and has sung in the School of Medicine's class show. She laughingly admits that her athletic abilities leave something to be desired, even though she plays intramural soccer on "the worst team in the whole school."

Scavone is one of 25 School of Medicine students to benefit from the Washington University Medical Scholars Loan Program. Hers is one of three named loans established by Elsie Boyles in memory of her late husband, Joe M. Boyles, M.D. '30. "We're all carrying such a huge amount of debt these days that an interest-free loan like this is greatly appreciated," Scavone says. "The fact that alumni have donated money to help us out has really boosted student morale."

Scavone, who plans to start a residency program in internal medicine next fall, came to Washington University from the University of Illinois at Champaign-Urbana, where she majored in biology and psychology. Although she describes her first two years at the School of Medicine as "too many lectures and too much memorization," she found herself really loving her third year on the wards. In addition to enjoying the interaction with patients and freedom to organize her own time, Scavone finds most of the attendings willing to take extra time to explain things. "It's that extra five minutes here and there that makes the difference," she explains.

Scavone has selected internal medicine as her specialty area because it is somewhat less focused than other specialties, allowing her to "keep my sights on the whole picture." She is looking forward to a four-week externship in London, where she will work in an intensive care unit. "It'll be interesting to compare the two philosophies (of socialized and private medicine)," she says. "I'll be spending about the same amount of time on the CCU unit at Jewish Hospital before I go."

Scavone sees the distribution of health care as the single most important challenge facing her generation of physicians. "A dichotomy of care is developing between the rich and poor," she says. "For example, this city has two magnetic resonance imaging facilities — one at the VA and one at Barnes. Yet there are people coming into the VA who are suffering from TB and cannot even afford to eat. What good is that technology to us, if we can't even solve endemic TB? We need to keep in mind that medicine is something for people." ■

When he was in fourth grade, Anthony C. Griffin, M.D. '87, wanted to play the drums. His parents couldn't afford to buy their son a drum set, however, so the young Griffin learned to play the trumpet on his cousin's coronet. He remembers his parents encouraging him to keep playing, even though, at one time, he wanted to quit. "They knew then that the trumpet was something I could enjoy for the rest of my life," he says. "From this I learned the value of not letting yourself quit just because you want to."

Today, more than a dozen years later, Griffin still plays the trumpet, while pursuing a passion for medicine that began almost as early as his first musical note. His initial fascination with medicine stemmed from frequent childhood visits to doctors, hospitals and clinics he made with his two asthmatic brothers. Once planted, his interest in medicine took root during high school when he participated in a science and health opportunities program sponsored by the University of Wisconsin, Madison.

When it came time for him to graduate, the high school football star from Kenosha, Wisconsin, who had already accumulated college credit, was a prime candidate for college recruiters. Griffin was offered scholarships at several prestigious institutions, among them the School of Music at the University of California–Berkeley. He decided upon Brown University because the ivy league school placed more emphasis on education than athletics.

During his freshman and sophomore years as a premed at Brown, Griffin played the receiving position on the football team. And during his sophomore year, he played the trumpet in a local jazz band. Now a senior medical student at Washington University, Griffin finds his soon-to-be alma mater similar to Brown in terms of its high degree of personability and support from administration and fellow students. He views his recent receipt of a named, free-interest loan as "testament to how concerned Washington University is in terms of its students." And he was impressed with the dinner that was held in conjunction with the establishment of the loans. "They could have just handed out the loans and said, 'Here you go.' It was just another example of how Washington University is a first class place."

Griffin plans to pursue a career in plastic surgery, remaining in St. Louis for his residency, so that he and his fiancée, Colette, a native of St. Louis, can marry this February. Surgery appeals to him because "it gives you the ability to intervene, to make direct applications to pathophysiology and obtain immediate personal gratification." And he believes plastic surgery suits him because, "it is so diverse, you can do anything from a face lift to tendon repair to reconstructive surgery. It's also technically appealing because it's so sophisticated."

Griffin would like to somehow contribute to medical research, having already spent a year investigating the role of glucotrienes in hydronephronic rabbit kidneys through the M.D./Master's program at the School of Medicine.

He most definitely believes that programs such as the Medical Scholars Loan Program will encourage current students to be good alums. "It has to start somewhere," he says. "Alumni coming back, alumni giving is what keeps it all going. It's that continuity that's so important." ■

"It was just another example of how Washington University is a first class place."

CLASS NOTES

'30s and '40s

Glen F. Irwin, M.D. '30, was selected by the Wisconsin Bureau of Tourism to have his color slide of a loon on the billboard advertising the tourism slogan, "Escape to Wisconsin." Dr. Irwin's slide was chosen from 100 other slides submitted to the bureau. A retired surgeon, Dr. Irwin and his wife, Jane, live on Planting Ground Lake, Wisconsin, where they are active loon watchers.

Cramer D. Reed, M.D. '41, has become director of an employee health management and fitness program called Health Strategies. A division of the Wesley Medical Center in Wichita, Kansas, the program features employee health promotion, cardiac rehabilitation, community health education and a 2,000-square foot fitness center.

James H. Cravens, M.D. '43, has been elected to a three-year term as president and chairman of the Illinois chapter of the American Academy of Pediatrics. The Illinois chapter is one of the largest in the academy, with more than 1,200 pediatrician members. Cravens has been a member of the Physicians and Surgeons Clinic in Quincy since 1948. He is also a member of the Academy's committee on hospital care, President of the Swanberg Medical Foundation of Adams County Medical Society, Past-President of the Adams County Medical Society and the Downstate Illinois Pediatric Society, a Diplomate of the American Board of Pediatrics and a Fellow in the American Academy of Pediatrics.

'50s and '60s

Oliver J. Biederman, M.D. '58, FHS, recently ran his twelfth marathon. He is currently the physician in charge of the Kaiser Permanente facility in Lancaster, California, where he emphasizes health maintenance and physical fitness.

C. Craig Tisher, M.D. '61, was recently elected to the Council of the American Society of Nephrology.

Anthony E. Fathman, M.D. '64, is serving a one-year term as president of the American College of Surgeons' Missouri chapter.

Roger L. Mell, M.D. '65, was recently elected Vice-President of the Southern Medical Association, a 50,000-member voluntary association of physicians dedicated to fostering scientific medicine.

Richard H. Weisbart, M.D., '65, was recently presented the Philip Hench Award by the Association of Military Surgeons of the United States for outstanding contributions in the field of rheumatology and arthritis. A professor of medicine at the University of California Los Angeles, and chief of rheumatology at the Veterans Administration Medical Center in Sepulveda, California, Weisbart is actively involved in human lymphokine research.

Jerome H. Kaplan, M.D. '66, was recently named one of 86 fellows by the American College of Radiology's Board of Chancellors.

'70s and '80s

Wendy R. Eider, M.D. '76, FHS, is in solo practice in rheumatology. She and her husband, **Barry D. Bernfeld, M.D. '77,** who is a surgeon, live in Yakima, Washington, with their three-and-a-half-year-old daughter, Jessica.

Faith H. Holcombe, M.D. '80, FHS, writes that she and her husband, Fred Fiedoreck Jr., M.D., a graduate of Harvard Medical School, are thrilled with their daughter, Elizabeth, who was born January 31st and "is already demonstrating a thirst for knowledge by chewing on our journals."

Robert W. Laakman, M.D. '80, FHS, is a partner in Radiology Associates P.A. in Little Rock, Arizona, where he lives with his wife, Sheree, and children: Pete, 3½, and Anna, two months.

IN MEMORIAM

Samuel D. Soule, M.D. '28, professor emeritus of clinical obstetrics and gynecology, died October 29, 1986, at the age of 82. A devoted faculty member, alum and community member, Soule served as chairman of the Dean's Committee at the School of Medicine for five years; as historian, correspondent and reunion chairman for his medical class; as chairman of the Alumni Relations Committee and as Vice President of the Alumni Association. He also was an Eliot Society member for many years.

Soule was on the staff of both Jewish and Barnes hospitals, having served as chief of obstetrics and gynecology and president at Jewish.

He contributed to more than 75 publications in his field and was a member of the American Medical Association, the Missouri Medical Association, the St. Louis Medical Society, the American College of Obstetricians and Gynecologists, the American Fertility Society, the American Society of Psychology, the Academy of Science of St. Louis, the St. Louis Gynecology Society and the Jewish Federation of St. Louis.

Mixing Medicine and History

BY CANDACE O'CONNOR

Emmet F. Pearson, M.D. '30, is a great believer in serendipity. "You do one thing," he likes to say, "and something else turns out better than you had expected." After all, he stored one antique physician's desk in his basement — and soon amassed a medical history collection. Then he helped plan a medical school for his hometown of Springfield, Illinois — and it provided the ideal framework for a new medical history museum named, in his honor, The Pearson Museum.

The 9-year-old museum pays tribute to the many physicians living and working in the upper Mississippi River basin, whose ingenuity and dedication have moved the field of medicine another halting step forward. Gleaming showcases in the large museum room, located on the SIU–Springfield campus, display some of their equipment. There are early X-ray tubes, ivory-handled bladder probes and intubation devices that saved the lives of children choking from diphtheria. A silver double button, invented by a Chicago surgeon in the 1890s, joined a resected intestine and sloughed off after healing.

"I'm sure that those who have an interest in medical history are much more appreciative of the wonderful things we have, which have been built on those things that have been discarded," says Pearson, emeritus professor of medical history, who has lectured extensively in the United States and Europe on medical history topics.

The museum is also a tribute to the vision of Pearson, a remarkable local physician who chose to bypass life in the big city for a successful career in Springfield. For more than 50 years, this 1930 Washington University School of Medicine graduate has maintained a private practice in internal medicine, while serving in such local leadership roles as Chairman of the Department of Medicine and President of Staff at Memorial Hospital. Along the way, as he modestly admits, he has been personal physician to two Illinois governors, one of them White House aspirant Adlai Stevenson.

"Dr. Pearson is an elder statesman of Springfield's medical community, held in high regard as a physician, teacher and community leader," says Jack Siefkas, former director of medical alumni and development programs, who met Pearson while working at SIU–Springfield. "Along

with being a role model, Dr. Pearson also has shown a warmth and charm to everyone associated with him."

As a founder and former president of the Sangamon County Historical Society, Pearson is deeply involved in historic preservation. A few years ago, he and his wife, Mary, discovered a century-old stagestop in nearby Clayville, restored it and presented it to Sangamon State University. He has long worked to give the Springfield area a broader view of itself. "Everything used to be Abraham Lincoln here. People feel that nothing happened before Lincoln came and nothing has happened since," he says.

But inevitably, he too has gotten caught up in Lincoln. In his museum, there are ledger pages showing Lincoln's purchases from a local drugstore. After careful research, Pearson has formed his own opinions about Lincoln's health. Lincoln was melancholic, covering up periods of depression by telling jokes; he had indigestion, which was never fully diagnosed. Most controversial of all, Pearson says, Lincoln may have had venereal disease.

Pearson was born in the hills of Tennessee near the Mississippi border. His father ran a country store and the family farm, formerly a plantation; his grandfather was a Confederate Civil War veteran, held prisoner by the "damn Yankees" in Memphis. "It was still a 19th century way of life: no electricity, no water works, no transportation except horse-drawn vehicles," he says.

After a year at the University of Mississippi, he followed his brother to Washington University, where Pearson finished his A.B. in 1926. To earn money, he worked in the cafeteria at night, climbing the ladder from dishwasher to cashier. During the summers, he supervised teams of magazine salesmen as they fanned out across the Midwest.

Pursuing a lifelong ambition, he moved on to the Washington University School of Medicine and an internship/residency at Barnes Hospital. The faculty was an eminent group; two won Nobel Prizes while he was there. He remembers particularly his mentors David Barr, M.D., Edmund Cowdry, M.D. and most of all, Evarts Graham, M.D., for whom he did research into the medical side of lung disease. "Many of my professors now have portraits on prominent walls at Barnes Hospital; they were such great physicians," he says.

> **"I'm sure that those who have an interest in medical history are much more appreciative of the wonderful things we have, which have been built on those things that have been discarded."**

Following medical school, Pearson used savings from his magazine job to finance a six-month trip to several famous European clinics. He admired the French treatment of nervous disorders and the German method of demonstrating patients, brought to perfection by Friedrich von Mueller, M.D.

Out of training in the midst of the Depression, Pearson picked Springfield, a state capitol with a reliable government payroll, as a place to settle down. He had specialized in internal medicine "since you get a philosophical point of view along with the scientific one, a 'holistic' approach." He made a fortunate choice of sub-specialty: the treatment of allergy. "No one had ever heard of it, so other doctors referred their patients to me," he says.

Then war exploded in the Pacific. Pearson had to leave his burgeoning practice and young family to spend four years at various military hospitals. A one-year stint as commander of a large hospital in the Philippines was the most harrowing. They cared for the Manila elite, including bishops and supreme court justices, along with wounded soldiers from the front lines just a few miles away.

Back home, he took a job at Northwestern University, only to decide within months that Chicago was "too big." He returned to Springfield and soon had prominent patients in Governor Adlai Stevenson and, later, Otto Kerner. "When Stevenson was running for the presidency, I was interviewed about his health," he recalls. "I always gave him a good report; I thought he was healthier than Eisenhower."

Before the 1968 state sesquicentennial, Pearson took on a fateful role as chairman of an Illinois State Medical Society committee setting up a medical history museum. They already had one item, a magnificent walnut desk, custom-made for a Chicago physician just before the great 1871 fire destroyed his office. Pearson stored it in his basement, only to discover that funds for the museum would not be available.

But medical history had been Pearson's long-time hobby. During medical school, he belonged to a group of interested students who met to discuss historical topics. On his way to Europe, he stopped at Johns Hopkins University and "sat at the feet" of the renowned William Welch, M.D., the first professor of medical history in the U.S.

Once his interest was rekindled, he started collecting — in earnest when space in the new medical school was assured. He acquired a complete antique drugstore with a sheaf of prescriptions and 207 apothecary jars bearing such intriguing labels as "myrrha," "pulvis rhei," or "crocus." He also began his own collection, now on display, of mail disinfected by various countries using smoke, formaldehyde or steam in an effort to stem epidemics.

The museum, which will soon expand to two new locations, also serves Pearson's favorite purpose: as a teaching forum for interested SIU medical students. Each year, some 10 percent of the student body studies medical history, writing papers on such topics as yellow fever epidemics or the late Chief Gray Eagle, a patient of Pearson's, who was the last Indian medicine man in Illinois.

Pearson still can't resist picking up an occasional museum piece. In their spare time, he and his wife travel or enjoy their four children and grandchildren. He shrugs off retirement. "I've been thinking about it for 20 years," he says, "but I don't get around to accomplishing it. I guess I like what I'm doing." ■

Outlook Gets High Marks

More than 20 years ago, when *Outlook* was first published as an eight-page newsletter, Dean M.K. King wrote, "We will begin modestly in size and scope, hoping for a more expansive future."

At that time, he invited alumni and members of the School of Medicine staff to send suggestions for the type of material to be contained in future issues, keeping in mind the publication's original goal: "to inform the staff, and also the alumni residing in St. Louis, of developments with which they are not already familiar."

To determine how well *Outlook* has been meeting its original goal and new goals as well, those responsible for *Outlook* once again solicited readers' suggestions — this time in the form of a four-page, mailed readership survey conducted last summer.

One-hundred-and-eighty-five readers responded to the survey, which was mailed to a total of 500 randomly selected recipients of the magazine. Of these respondents, 36 percent were M.D. alums, 16 percent were former house staff, 13 percent were School of Nursing graduates, 10 percent were allied health graduates, 7 percent were health administration and planning graduates, 6 percent were faculty members and the remaining 18 percent included Ph.D. alums, M.S.T.P. alums, non-academic staff and students and their parents.

These readers gave *Outlook* magazine high marks for overall quality and appearance. Sixty-seven percent rated the overall quality of *Outlook* as excellent, and 28 percent rated it as good. The magazine was rated even more highly for its appearance, with 80 percent of the respondents marking excellent, and 45 percent good. At least 90 percent of the respondents gave *Outlook* good or excellent ratings for quality of writing, photography and illustrations.

Outlook's coverage of basic research, clinical research and patient care was evaluated as excellent or good by at least 80 percent of the respondents, while more than half gave the magazine good or excellent ratings for its coverage of students, general issues in academic medicine, institutional additions, alumni, faculty or institutional changes, opinion and development. The publication's coverage of nostalgia and curriculum and education were rated as needing improvement, with more than one-quarter of the respondents evaluating coverage of these topics as fair or poor. Survey results also included a significant number of written-in suggestions to provide more coverage of nursing and other allied health fields.

Survey respondents marked feature stories as the section they read the most, followed by Newsbriefs, Class Notes, Alumni Report, Silhouette, Personal Outlook and Student Stage.

Readers' enjoyment of *Outlook* appears to depend to a large extent upon its visual effect. Ninety-six percent of the respondents marked that the color photographs and illustrations enhance the magazine, and 53 percent admitted that these photos and illustrations usually entice them to read a particular story. The most frequently marked reason for reading a given story, however, was that "it regards a topic that interests me."

Outlook's readers appear to be satisfied with how often it comes out, with approximately 90 percent of the respondents marking that the magazine should continue to be published on a quarterly basis.

Seventy percent of the respondents prefer feature articles that focus exclusively on research and people at Washington University, while the remaining 30 percent would like *Outlook* to include stories about people and research outside the university. Almost three-quarters of the respondents, however, agreed that they prefer more and shorter stories per issue, so that they can see a wider range of topics.

On the whole, the *Outlook* survey found its readers to be proud of the publication. Approximately 68 percent of the respondents marked that they share the magazine with a friend or family member at least occasionally.

As survey results indicate, Outlook has certainly come a long way from its humble beginnings, with major strides having been made in the last three years under the direction of former editor Suzanne Hagan. Those who continue to be responsible for the magazine's production hope to make it an even greater success in the future. Readers' suggestions for a greater variety of topics and more shorter stories have been well taken, and the importance of the publication's visual appeal also has been noted. *Outlook's* new editor, Kathy Will, who comes to the magazine from Northwestern University Medical School where she was associate editor of the alumni magazine, will be working hard to make *Outlook* even better with each new issue.

—The Office of Medical Public Relations

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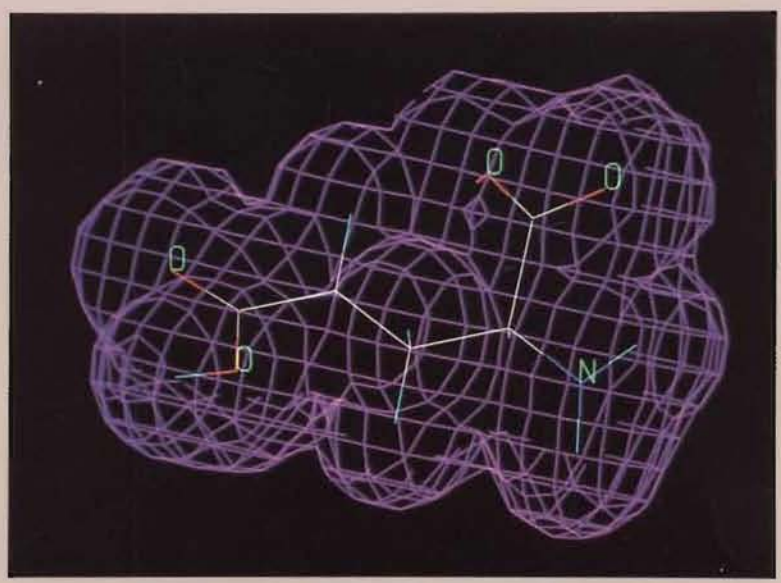

Glutamate, which is found in high concentrations in the brain, is a paradoxical molecule, not only serving as a neurotransmitter and a major building block for the formation of important brain peptides and proteins, but also as a potential toxin. Studying the Jekyll and Hyde properties of glutamate are Washington University School of Medicine's own Drs. John W. Olney and Madelon T. Price. *See story, page 8.*